STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 151858

TO: Amy H Bowman **Location: REM-2C18** **Art Unit: 1635** **Monday, May 09, 2005** **Case Serial Number: 09/428458**	**From: Alex Waclawiw** **Location: Biotech-Chem Library** **CM1-6A02** **Phone: 308-4491** **Alexandra.waclawiw@uspto.gov**

Search Notes

151858

STIC-Biotech/ChemLib

From: Bowman, Amy
Sent: Wednesday, April 27, 2005 2:06 PM
To: STIC-Biotech/ChemLib
Cc: Bowman, Amy
Subject: search for application 09/428,458

Hello,
I need a search for application 09/428,458. Specifically, I need a search for any thio-substituted cAMP analog which is an equatorial diastereomer of 8-substituted 3',5' cyclic adenosine monophosphorothioate. The key is that I not only need the compound, but I only need art for such compounds administered to any subject in vivo.
I have found some art on the compound, but not on administration of such compounds in vivo, as required by claim 45.
Thank you,
Amy Bowman
AU 1635
REM 2C18
571-272-0755

****
STAFF USE ONLY
Searcher:_____
Searcher Phone: 2-
Date Searcher Picked up:____ 5-5-05
Date Completed:_____ 5-9-05
Searcher Prep/Rev. Time:__16
Online Time:_____ 68

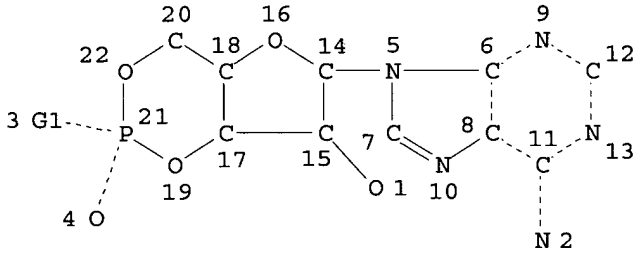
Point of Contact:
Alexandra Waclawiw
Technical Info. Specialist
CM1 6A02 Tel: 308-4491

****
Type of Search
NA#:_____ AA#:_____
Interference:____ SPDI:___
S/L:_____ Oligomer:_____
Encode/Transl:_____
Structure#:_____ Text:___
Inventor:____ Litigation:___

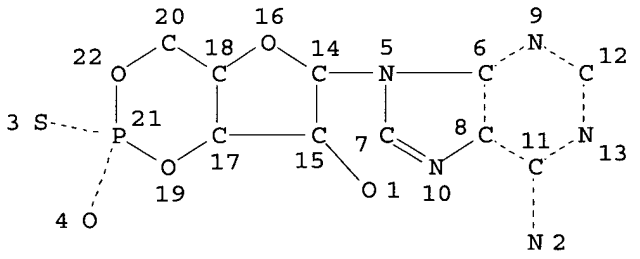
****
Vendors and cost where applicable
STN:_____
DIALOG:_____
QUESTEL/ORBIT:_____
LEXIS/NEXIS:_____
SEQUENCE SYSTEM:_____
WWW/Internet:_____
Other(Specify):_____

```
=> d his

     (FILE 'HCAPLUS' ENTERED AT 11:40:12 ON 09 MAY 2005)
               DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 11:40:17 ON 09 MAY 2005
               ACT BOWMAN/A
               ---------
L1             STR
L2           955 SEA FILE=REGISTRY SSS FUL L1
               ---------
               ACT BOWMAN2/A
               ---------
L3             STR
L4   (        955)SEA FILE=REGISTRY SSS FUL L3
L5             STR
L6            63 SEA FILE=REGISTRY SUB=L4 SSS FUL L5
               ---------

     FILE 'HCAPLUS' ENTERED AT 11:40:55 ON 09 MAY 2005
L7           201 S L6
L8        396256 S VIVO
L9             7 S L8 AND L7
L10           69 S L7 (L)  (BAC OR THU)/RL
L11           34 S L10 AND (63 OR 1)/SC,SX
L12           10 S L10 AND DRUG DELIVER?
L13           35 S L11 OR L12

     FILE 'WPIDS' ENTERED AT 11:48:25 ON 09 MAY 2005

     FILE 'HCAPLUS' ENTERED AT 11:50:56 ON 09 MAY 2005

     FILE 'WPIDS' ENTERED AT 11:52:30 ON 09 MAY 2005
               E WO9848809/PN
L14           11 S ?PHOSPHOROTHIOATE? (S) (CYCLIC (3A) ADENOSINE OR CAMP)
L15           14 S ?PHOSPHOROTHIOATE? (L) (CYCLIC (3A) ADENOSINE OR CAMP)
L16           13 S L15 AND (VIVO OR THERAP? OR TREAT? OR DELIVER?)
L17           16 S ?PHOSPHOROTHIOATE? AND (CYCLIC (3A) ADENOSINE OR CAMP)
L18           15 S L17 AND (VIVO OR THERAP? OR TREAT? OR DELIVER? )

     FILE 'WPIDS, HCAPLUS' ENTERED AT 12:17:29 ON 09 MAY 2005
L19           43 DUP REM L18 L13 (7 DUPLICATES REMOVED)
```

```
=> fil wpids hcaplus
FILE 'WPIDS' ENTERED AT 12:18:42 ON 09 MAY 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION

FILE 'HCAPLUS' ENTERED AT 12:18:42 ON 09 MAY 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

=> d que l19
L3                STR
```




```
VAR G1=O/S
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  22

STEREO ATTRIBUTES: NONE
L4   (       955)SEA FILE=REGISTRY SSS FUL L3
L5                STR
```




```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  22

STEREO ATTRIBUTES: NONE
L6            63 SEA FILE=REGISTRY SUB=L4 SSS FUL L5
L7           201 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6
L10           69 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 (L)  (BAC OR THU)/RL
L11           34 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND (63 OR 1)/SC,SX
L12           10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND DRUG DELIVER?
```

Structures W/ Thio

L13 35 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 OR L12
L17 16 SEA FILE=WPIDS ABB=ON PLU=ON ?PHOSPHOROTHIOATE? AND (CYCLIC (3A) ADENOSINE OR CAMP)
L18 15 SEA FILE=WPIDS ABB=ON PLU=ON L17 AND (VIVO OR THERAP? OR TREAT? OR DELIVER?)
L19 43 DUP REM L18 L13 (7 DUPLICATES REMOVED)

L19 ANSWER 1 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN DUPLICATE 1
ACCESSION NUMBER: 2004-662346 [64] WPIDS
CROSS REFERENCE: 2003-111976 [10]; 2003-393509 [37]; 2003-450982 [43]; 2003-779129 [73]; 2004-635468 [61]; 2004-748573 [73]; 2004-805123 [79]; 2004-833580 [82]; 2005-101299 [11]; 2005-132260 [14]
DOC. NO. CPI: C2004-236529
TITLE: Isolated, purified or recombinant complex, useful for identifying an antiviral, anti-apoptotic or anti-cancer, comprising POSH polypeptide and POSH-associated protein (POSH-AP).
DERWENT CLASS: B04 B05 D16
INVENTOR(S): ALROY, I; BEN-AVRAHAM, D; GREENER, T; REISS, Y; TAGLICHT, D N; TUVIA, S; YAAR, L
PATENT ASSIGNEE(S): (PROT-N) PROTEOLOGICS INC
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004078130	A2	20040916	(200464)*	EN	374

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004078130	A2	WO 2004-US6308	20040302

PRIORITY APPLN. INFO: US 2004-549896P 20040302; US
2003-451437P 20030303; US
2003-452284P 20030305; US
2003-455760P 20030319; US
2003-456640P 20030320; US
2003-460526P 20030403; US
2003-460792P 20030404; US
2003-464285P 20030421; US
2003-469462P 20030509; US
2003-471378P 20030515; US
2003-472327P 20030520; US
2003-474706P 20030530; US

2003-475825P	20030603; US
2003-479317P	20030617; US
2003-480215P	20030619; US
2003-480376P	20030619; US
2003-493860P	20030808; US
2003-498634P	20030828; US
2003-503931P	20030916; WO
2003-US35712	20031110; WO
2004-US3600	20040205

AB WO2004078130 A UPAB: 20050228

NOVELTY - An isolated, purified or recombinant complex (I) comprising a POSH polypeptide and a POSH-associated protein (POSH-AP) (a) or HERPUD1 and a Ubiquitin ligase (b), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) identifying (M1) an agent that modulates an activity of a POSH polypeptide or POSH-AP, by identifying an agent that disrupts (I)-(a), where the agent that disrupts (I)-(a) is an agent that modulates an activity of the POSH polypeptide or the POSH-AP;

(2) identifying (M2) an antiviral agent, comprising identifying a test agent that disrupts (I)-(a), and evaluating the effect of the test agent on a function of a virus, or identifying a test agent that inhibits an activity of or expression of a POSH-AP and evaluating effect of the test agent on a function of a virus;

(3) identifying (M3) an anti-apoptotic agent, comprising identifying a test agent that disrupts (I)-(a) and evaluating the effect of the test agent on apoptosis of a cell, where the agent that decreases apoptosis of the cell is an anti-apoptotic agent;

(4) identifying (M4) an anti-cancer agent, comprising identifying a test agent that disrupts (I)-(a), and evaluating the effect of the test agent on proliferation or survival of a cancer cell, where the agent that decreases proliferation or survival of a cancer cell is an anti-cancer cell;

(5) identifying (M5) an agent that inhibits trafficking of a protein through the secretory pathway, comprising identifying a test agent that disrupts (I)-(a), and evaluating the effect of the test agent on the trafficking of a protein through the secretory pathway, where the agent that disrupts localization of the POSH-AP is an agent that inhibits trafficking of a protein through the secretory pathway;

(6) identifying (M6) an agent that inhibits the progression of a neurological disorder, comprising identifying a test agent that disrupts (I)-(a), and evaluating the effect of the test agent on the trafficking of a protein through the secretory pathway, where the agent that disrupts localization of a POSH-AP is an agent that inhibits progression of a neurological disorder, or evaluating the effect of the test agent on the ubiquitination of a protein;

(7) **treating** (M7) a viral infection in a subject in need of **treatment**, comprising administering an agent that inhibits a POSH-AP or an agent that inhibits MSTP028 in an amount sufficient to inhibit the viral infection;

(8) use of protein kinase A inhibitor, inhibitor of HERPUD1 or MSTP028 for the manufacture of medicament for **treatment** of viral infection;

(9) a packaged pharmaceutical (II) for use in **treating** a viral infection comprising pharmaceutical composition comprising an inhibitor of POSH-AP and a carrier, and instructions for use;

(10) evaluating (M8) an antiviral agent, by providing a test agent that inhibits an activity of or expression of a POSH-AP and evaluating an effect of the test agent on a function of a virus;

(11) identifying (M9) an agent that modulates a POSH function, by

identifying an agent that modulates a POSH-AP and testing the effect of the agent on a POSH function;

(12) evaluating (M10) an agent that modulates a POSH function, by providing an agent that modulates a POSH-AP and testing the effect of the agent on POSH function;

(13) identifying (M11) an agent that modulates a HERPUD1 function, by identifying an agent that modulates POSH and testing the effect of the agent on a HERPUD1 function;

(14) evaluating (M12) an agent that modulates a HERPUD1 function, by providing an agent that modulates POSH and testing the effect of the agent on a HERPUD1 function;

(15) inhibiting (M13) an activity of a POSH-AP in a cell, by contacting the cell with an inhibitor of POSH;

(16) **treating** (M14) a POSH-associated disease in a subject, by administering a POSH-AP inhibitor to a subject in need of the **treatment**;

(17) identifying (M15) an anti-viral agent or identifying a modulator of POSH, by forming a mixture comprising POSH polypeptide, POSH-AP, and a test agent, and detecting phosphorylation of the POSH polypeptide, where an agent that inhibits phosphorylation of the POSH is an anti-viral agent, or forming a mixture comprising POSH polypeptide, POSH-AP, ubiquitin and a test agent and detecting ubiquitination of the POSH-AP, where an agent that inhibits ubiquitination of the POSH is an anti-viral agent;

(18) **treating** or preventing (M16) a POSH associated cancer in a subject, by administering an agent that inhibits a POSH-AP;

(19) **treating** or preventing (M17) POSH-associated neurological disorder in a subject, by administering an agent that inhibits a POSH-AP or ubiquitin ligase activity of POSH; and

(20) **treating** (M18) a neurological disorder, by administering an agent that inhibits the ubiquitination of a POSH-AP.

ACTIVITY - Cytostatic; Nootropic; Neuroprotective; Antiparkinsonian; Anticonvulsant; Antiviral; Neuroleptic; CNS-Gen.

MECHANISM OF ACTION - Inhibitor of POSH (claimed).

HeLa SS6 cells were transfected with either control or POSH-specific small interference (si)RNA. Cells were subsequently infected with West Nile Virus (WNV) (4 multiply 104 plaque forming units (PFU)/well). Viruses were harvested 24 hours and 48 hours post-infection, serially diluted, and used to infect Vero cells. As a control WNV (4 multiply 104 PFU/well) that was not passed through HeLaSS6 cells, was used to infect Vero cells. Virus titer was determined by plaque assay in vero cells. Virus titer was reduced by 2.5-log in cells **treated** with POSH-specific siRNA relative to cells transfected with control siRNA.

USE - (M1) is useful for identifying an agent that modulates an activity of a POSH polypeptide or POSH-AP. (M2) is useful for identifying an antiviral agent. (M3) is useful for identifying an anti-apoptotic agent. (M4) is useful for identifying an anti-cancer agent. (M5) is useful for identifying an agent that inhibits trafficking of a protein through the secretory pathway. (M6) is useful for identifying an agent that inhibits the progression of a neurological disorder. (M7) is useful for **treating** a viral infection. (M9) is useful for identifying an agent that modulates a POSH function. (M11) is useful for identifying an agent that modulates a HERPUD1 function. (M13) is useful for inhibiting an activity of a POSH-AP in a cell. (M14) is useful for **treating** a POSH-associated disease in a subject. The POSH-associated disease is viral infection, POSH-associated cancer or POSH-associated neurological disorder. (M15) is useful for identifying an anti-viral agent or identifying a modulator of POSH. (M16) is useful for **treating** or preventing a POSH associated cancer in a subject. (M17) is useful for **treating** or preventing POSH-associated neurological disorder in a subject. (M18) is useful for **treating** a neurological disorder

e.g. Alzheimer's disease, Parkinson's disease, Huntington's disease, schizophrenia, Niemann-Pick's disease. (All claimed.)
Dwg.0/36

L19 ANSWER 2 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN DUPLICATE 2
ACCESSION NUMBER: 2004-635468 [61] WPIDS
CROSS REFERENCE: 2003-111976 [10]; 2003-393509 [37]; 2003-450982 [43]; 2003-779129 [73]; 2004-662346 [64]; 2004-748573 [73]; 2004-805123 [79]; 2004-833580 [82]; 2005-101299 [11]; 2005-132260 [14]
DOC. NO. CPI: C2004-228371
TITLE: New complex comprising a Plenty Of SH3 (POSH) polypeptide and a POSH-associated kinase (POSH-AK) or its subunit, useful in preparing a composition for **treating** or preventing a POSH associated cancer.
DERWENT CLASS: B04 D16
INVENTOR(S): ALROY, I; REISS, Y; TAGLICHT, D N; TUVIA, S; YAAR, L
PATENT ASSIGNEE(S): (PROT-N) PROTEOLOGICS INC
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004073609	A2	20040902	(200461)*	EN	163

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004073609	A2	WO 2004-US3600	20040205

PRIORITY APPLN. INFO: US 2003-503931P 20030916; US 2003-445534P 20030205; US 2003-451437P 20030303; US 2003-464285P 20030421

AB WO2004073609 A UPAB: 20050228
NOVELTY - An isolated, purified or recombinant complex comprising a Plenty Of SH3 (POSH) polypeptide and a POSH-associated kinase (POSH-AK) or its subunit, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) identifying an agent that modulates an activity of a POSH polypeptide or POSH-AK;
(2) identifying an antiviral agent;
(3) identifying an anti-apoptotic agent;
(4) identifying an anti-cancer agent;
(5) identifying an agent that inhibits trafficking of a protein through the secretory pathway;
(6) **treating** a viral infection in a subject;
(7) a packaged pharmaceutical for **treating** a viral infection comprises a pharmaceutical composition comprising an inhibitor of a POSH-AK and a carrier and instructions for use;
(8) evaluating an antiviral agent;

(9) identifying an agent that modulates a POSH function;
(10) evaluating an agent that modulates a POSH function;
(11) identifying an agent that modulates a protein kinase A (PKA) function;
(12) evaluating an agent that modulates a PKA function;
(13) identifying an agent that modulates a JNK pathway function;
(14) evaluating an agent that modulates a JNK pathway function;
(15) inhibiting the Jun kinase (JNK) pathway in a human cell;
(16) inhibiting an activity of a PKA in a cell;
(17) **treating** a JNK pathway-associated disease in a subject;
(18) **treating** a PKA associated disease in a subject;
(19) identifying a modulator of POSH;
(20) enhancing interaction of a POSH polypeptide with a second protein in a cell;
(21) inhibiting ubiquitination activity of a POSH polypeptide in a cell;
(22) **treating** or preventing a POSH associated cancer in a subject;
(23) an isolated, purified or recombinant phosphorylated POSH polypeptide;
(24) preparing a phosphorylated POSH polypeptide; and
(25) a portion of a POSH polypeptide consisting essentially of 15 to 100 consecutive amino acids of a mammalian POSH polypeptide which include a consensus PKA phosphorylation site.

ACTIVITY - Cytostatic; Virucide.
No biological data given.
MECHANISM OF ACTION - Vaccine.
USE - The complex comprising a Plenty Of SH3 (POSH) polypeptide and a POSH-associated kinase (POSH-AK) or its subunit is useful in preparing a composition for treating or preventing a POSH associated cancer. The protein kinase A (PKA) inhibitor is useful for the manufacture of a medicament for treating a viral infection. (All claimed.)
Dwg.0/31

L19 ANSWER 3 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN DUPLICATE 3
ACCESSION NUMBER: 2004-357143 [33] WPIDS
DOC. NO. CPI: C2004-135592
TITLE: Composition useful for **treatment** of autoimmune disease or condition e.g. primary myxoedema, comprising agent which raises **cAMP** concentration in monocyte cell, and granulocyte-macrophage colony stimulating factor or its derivative.
DERWENT CLASS: B05
INVENTOR(S): KELLY, R W
PATENT ASSIGNEE(S): (MEDI-N) MEDICAL RES COUNCIL
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004035083	A2	20040429	(200433)*	EN	92

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

AU 2003274342 A1 20040504 (200467)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004035083	A2	WO 2003-GB4537	20031021
AU 2003274342	A1	AU 2003-274342	20031021

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003274342	A1 Based on	WO 2004035083

PRIORITY APPLN. INFO: GB 2002-24415 20021021

AB WO2004035083 A UPAB: 20040525

NOVELTY - A composition or a **therapeutic** system comprises an agent (A1) which raises **cAMP** concentration in a monocyte cell, and granulocyte-macrophage colony stimulating factor (GMCSF) or its derivative and optionally a carrier, diluent or excipient.

ACTIVITY - Immunosuppressive; Antianemic; Anabolic; Hypertensive; Antidiabetic; Nephrotropic; Muscular Gen.; Neuroprotective; Ophthalmological; Antiinflammatory; Antiulcer; Gastrointestinal Gen.; Dermatological; CNS Gen.; Antiarthritic; Antirheumatic; Thyromimetic; Antithyroid; Vasotropic; Antiallergic; Antiasthmatic; Virucide; Cytostatic.

MECHANISM OF ACTION - Granulysin expression stimulator; Interleukin-10 expression stimulator.

USE - In the manufacture of a medicament for the **treatment** of autoimmune disease or condition (e.g. primary myxoedema, thyrotoxicosis, pernicious anemia, autoimmune atrophic gastritis, Addison's disease, insulin dependent diabetes mellitus, Goodpasture's syndrome, myasthenia gravis, sympathetic ophthalmia, multiple sclerosis, autoimmune hemolytic anemia, idiopathic leucopenia, ulcerative colitis, dermatomyositis, scleroderma, mixed connective tissue disease, rheumatoid arthritis, irritable bowel syndrome, systemic lupus erythematosus, Hashimoto's disease, thyroiditis, Behcet's disease, celiac disease/dermatitis heroetiformis, renal vasculitis and demyelinating disease), allergic diseases such as allergic asthma, for inducing tolerance to an antigen in a patient or **treating** an aberrant or undesired immune or inflammatory response (e.g. deficiency in interleukin -10 production) to the antigen in the patient, for **treating** diseases associated with transplant rejection (e.g. graft versus host disease or host versus graft disease), viral infection (e.g. herpes simplex virus infection (such as cold sore) and human papillomas virus infection (e.g. wart)) and tumors (all claimed).

ADVANTAGE - The composition stimulates or enhances granulysin expression in cells of the macrophage/monocyte lineage, and particularly stimulates or enhances interleukin-10 expression in, and secretion from cells of, the macrophage/monocyte lineage.

Dwg.0/9

L19 ANSWER 4 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN DUPLICATE 4

ACCESSION NUMBER: 2004-472124 [45] WPIDS

DOC. NO. CPI: C2004-177150

TITLE: Skin barrier function recovery promoter for screening and improving recovery of skin barrier function in mammals, contains compound suppressing activity or production of intracellular cyclic AMP.

DERWENT CLASS: B05

PATENT ASSIGNEE(S): (SHIS) SHISEIDO CO LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 2004175687	A	20040624	(200445)*		16

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 2004175687	A	JP 2002-340804	20021125

PRIORITY APPLN. INFO: JP 2002-340804 20021125

AB JP2004175687 A UPAB: 20040716
NOVELTY - A skin barrier function recovery promoter contains a compound which suppresses activity or production of intracellular cyclic AMP (**cAMP**).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) screening of skin barrier function recovery promoting compound, which involves acting the compound on mammalian cell and measuring reduction in concentration of intracellular **cAMP** by the action of the compound after appropriate time; and

(2) skin improvement method, which involves applying a skin external preparation containing the compound suppressing activity or production of intracellular **cAMP** and recovering the skin barrier function of the applied skin.

ACTIVITY - Dermatological.

MECHANISM OF ACTION - Activity or Production of **cAMP** suppressor. Epidermis of hairless mouse was applied with 200 micro l of aqueous solution containing 1mM of **cAMP** Rp ((R)-**adenosine**, **cyclic** 3',5'-(hydrogen **phosphorothioate**) tri ethyl ammonium)) and maintained for 48 hours. Para formaldehyde, paraffin, hematoxylin and eosin solution were sequentially added and recovery of skin barrier function by suppressing **cAMP** activity was evaluated according to Elias P. M. et al, Skin Pharmacol. Appl. Skin Physiol. 14: S28-34, 2001. A control was performed with water. The histological results showed that the test group had excellent recovery against skin barrier function, than the control.

USE - For screening and improving recovery of skin barrier function (claimed) in mammals useful in **treating** roughness of skin caused by dermatological disorders, such as atopic dermatitis, contact dermatitis and psoriasis.

ADVANTAGE - The novel skin barrier function recovery promoter enables screening of skin barrier function recovery in mammals, decreases amount of percutaneous moisture content transpiration, improves recovery of skin barrier function by suppressing activity of **cAMP** and restraining inflow of calcium ion into cell, improves thickness of skin and inhibits proliferation of abnormal epidermal skin/layer.

DESCRIPTION OF DRAWING(S) - The figure shows graph depicting relationship between **cAMP** antagonist and skin barrier function recovery. (Drawing includes non-English language text).

Dwg.2/8

L19 ANSWER 5 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:453015 HCAPLUS
DOCUMENT NUMBER: 141:17632

TITLE: Methods and agents elevating cAMP and calcium ion for increasing neurogenesis
INVENTOR(S): Bertilsson, Goran; Erlandsson, Rikard; Frisen, Jonas; Haegestrand, Anders; Heidrich, Jessica; Hellstrom, Kristina; Haggblad, Johan; Jansson, Katarina; Kortesmaa, Jarkko; Lindquist, Per; Lundh, Hanna; McGuire, Jacqueline; Mercer, Alex; Njberg, Karl; Ossoinak, Amina; Patrone, Cesare; Ronnholm, Harriet; Zachrisson, Olof; Wikstrom, Lilian
PATENT ASSIGNEE(S): Neuronova AB, Swed.
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004045592	A2	20040603	WO 2003-IB5311	20031120
WO 2004045592	A3	20041104		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

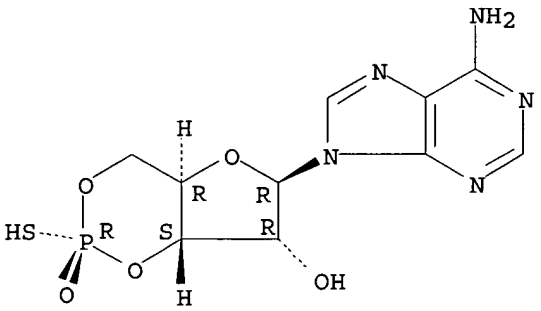
PRIORITY APPLN. INFO.: US 2002-427912P P 20021120

AB The invention discloses methods for promoting neurogenesis by contacting neuronal tissue with intracellular cAMP-elevating agents and intracellular calcium ion-elevating agents. Agents for promoting neurogenesis are also disclosed.

IT **73208-40-9**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cAMP-elevating and calcium ion-elevating compds. for increasing neurogenesis)

RN 73208-40-9 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 6 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:41100 HCAPLUS
DOCUMENT NUMBER: 140:99691
TITLE: Methods and compounds for reducing biofilm formation
INVENTOR(S): Romeo, Tony; Jackson, Debra W.; Simecka, Jerry W.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 13 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004009927	A1	20040115	US 2003-438255	20030513
WO 2004006832	A2	20040122	WO 2003-US15349	20030513
WO 2004006832	A3	20040401		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

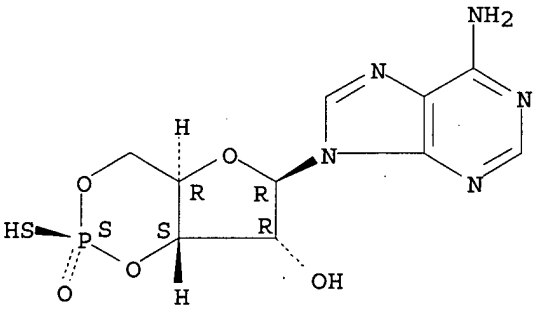
PRIORITY APPLN. INFO.: US 2002-379413P P 20020513

AB The invention relates to methods and compns. for modulating biofilm formation by bacteria. In particular, the invention provides a method for reducing biofilm formation by bacteria comprising administering a control agent wherein the control agent is glucose, a glucose analog, an adenylate cyclase inhibitor, a phosphodiesterase inhibitor, or a IIAGlc dephosphorylation stimulator. The invention also provides a method for enhancing biofilm formation by bacteria comprising administering cAMP or a cAMP analog.

IT **71774-13-5 73208-40-9**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods and compds. for reducing biofilm formation)

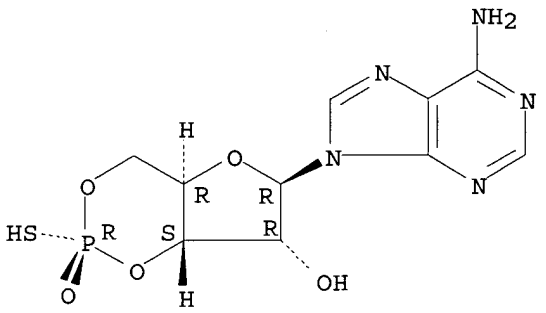
RN 71774-13-5 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 73208-40-9 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 7 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN DUPLICATE 5
ACCESSION NUMBER: 2004-122230 [12] WPIDS
DOC. NO. NON-CPI: N2004-097913
DOC. NO. CPI: C2004-048949
TITLE: Detecting a senescent cell, useful for **treating** diseases associated with senescence (e.g. atherosclerosis), comprises measuring a relative alteration to young cell in a signal or molecular species involved in signal transduction.
DERWENT CLASS: B04 B05 D16 S03
INVENTOR(S): JANG, I; PARK, S; YEO, E
PATENT ASSIGNEE(S): (META-N) METABOLIC ENG LAB CO LTD
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003104482	A1	20031218	(200412)*	EN	92
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					
AU 2002303023	A1	20031222	(200445)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003104482	A1	WO 2002-KR1067	20020605
AU 2002303023	A1	AU 2002-303023	20020605
		WO 2002-KR1067	20020605

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002303023	A1 Based on	WO 2003104482

PRIORITY APPLN. INFO: WO 2002-KR1067 20020605
AB WO2003104482 A UPAB: 20040218
NOVELTY - Detecting a senescent cell comprises measuring a relative alteration to young cell in a signal or molecular species involved in signal transduction, is new.
DETAILED DESCRIPTION - Detecting a senescent cell comprises measuring a relative alteration to young cell in a signal or molecular species involved in signal transduction selected from:
(a) a reduction in Ca2+ oscillation;
(b) a reduction in expression of F-actin;
(c) a reduction in activity of phospholipase C or D;
(d) a reduction in expression or phosphorylation of platelet-derived growth factor (PDGF) receptor;
(e) a reduction in phosphorylation of phospholipase C- gamma 1;
(f) a reduction in expression of phospholipase D1;
(g) a reduction in EDG-2, EDG-7, Gi1, Gi2 or Gi3;
(h) a reduction in activity or expression of phosphodiesterase; and
(i) an increase in activity or expression of adenylyl cyclase or protein kinase A, in activity of protein kinase C, in phosphorylation of CREG, or in **cAMP** content.
INDEPENDENT CLAIMS are also included for the following:
(1) a method for modulating cellular senescence, comprising **treating** a senescent cell with an amount of an inhibitor of adenylyl cyclase, an inhibitor of protein kinase A, an inhibitor of protein kinase C or an activator of Gi protein; and
(2) a composition for modulating cellular senescence of a senescent cell, comprising an amount of an inhibitor of adenylyl cyclase, an inhibitor of protein kinase A, an inhibitor of protein kinase C or an activator of Gi protein.
ACTIVITY - Antiparkinsonian; Neuroprotective; Nootropic; Anticonvulsant; Cerebroprotective; Osteopathic; Endocrine-Gen.; Antiarteriosclerotic; Thrombolytic; Ophthalmological; Dermatological.
No biological data given.
MECHANISM OF ACTION - Adenylyl Cyclase Inhibitor; Protein Kinase Inhibitor-A; Protein Kinase Inhibitor-C; G-Protein Stimulator.
USE - The composition and methods are useful in detecting and modulating cellular senescence or in **treating** diseases or conditions associated with senescence, such as Parkinson's disease, Alzheimer's disease, Huntington's disease, stroke, osteoporosis, hair loss, atherosclerosis, calcification, thrombosis, macular degeneration, wrinkling or aging. These may also be used in identifying substances affecting cellular senescence.
Dwg.0/21

L19 ANSWER 8 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN DUPLICATE 6
ACCESSION NUMBER: 2004-062302 [06] WPIDS
DOC. NO. CPI: C2004-025590
TITLE: Use of deoxyadenosine derivatives for the manufacture of a medicament the **treatment** of human diseases e.g. cancer, chronic inflammation, thrombosis, type-2-diabetes mellitus.
DERWENT CLASS: B04
INVENTOR(S): BOS, J; CHRISTENSEN, A; DE KONING, J; DOSKELAND, S; GENIESER, H G; SCHWEDE, F
PATENT ASSIGNEE(S): (KYLI-N) KYLIX BV
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

```
-----------------------------------------------
WO 2003104250   A1 20031218 (200406)* EN   95
   RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
       LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
    W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
       DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
       KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
       RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA
       ZM ZW
AU 2003242672   A1 20031222 (200445)
EP 1511757      A1 20050309 (200518)  EN
    R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
       MC MK NL PT RO SE SI SK TR
```

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003104250	A1	WO 2003-EP6120	20030610
AU 2003242672	A1	AU 2003-242672	20030610
EP 1511757	A1	EP 2003-757062	20030610
		WO 2003-EP6120	20030610

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003242672	A1 Based on	WO 2003104250
EP 1511757	A1 Based on	WO 2003104250

PRIORITY APPLN. INFO: EP 2002-77219 20020607

AB WO2003104250 A UPAB: 20040123

NOVELTY - Using deoxyadenosine derivatives, their deaza-analogues, salts, esters, and/or solvates for the manufacture of a medicament the **treatment** of human diseases, is new.

DETAILED DESCRIPTION - Using deoxyadenosine derivatives of formula (I), their deaza-analogues, salts, esters, and/or solvates for the manufacture of a medicament the **treatment** of human diseases.

R1 = H, halo, azide, alkyl, aryl, amide-alkyl, amide-aryl, OH, O-alkyl, O-aryl, SH, S-alkyl, S-aryl, SeH, Se-alkyl, Se-aryl, amino, NH-alkyl, NH-aryl, N-bisalkyl, N-bisaryl or cycloalkylamino;

R2 = H, halo, azide, O-alkyl, S-alkyl, Se-alkyl, NH-alkyl, N-bisalkyl, alkyl-carbamoyl, cycloalkylamine or silyl;

R3 = H, halo, OH, azide, amidoalkyl, amide-aryl, O-alkyl, O-aryl, SH, S-alkyl, S-aryl, amino, NH-alkyl, NH-aryl, N-bisalkyl, N-bisaryl, NH-alkyl-carbamoyl or cycloalkylamino;

R4 and R5 = OH, SH or T; and

T = OH, SH, amino, H, alkyl, O-alkyl, O-aryl, S-alkyl, S-aryl, NH-alkyl, NH-aryl, N-bisalkyl or N-bisaryl.

Provided that when R4 is OH or SH then R5 is T; and when R5 is OH or SH then R4 is T.

An INDEPENDENT CLAIM is also included for compound of formula (I) (excluding 2'-deoxyadenosine-3',5'-cyclic monophosphate, N6-monobutyryl-2'-deoxyadenosine-3',5'-cyclic monophosphate, 2'-deoxyadenosine-3',5'-cyclic **monophosphorothioate**, 2'-deoxyadenosine-3',5'-cyclic monophosphoroanilidate, 2'-deoxyadenosine-3',5'-cyclic monophosphate methyl triester, 2'-deoxyadenosine-3',5'-cyclic monophosphate ethyl triester, 2'-O-methyladenosine-3',5'-cyclic monophosphate, 2'-O-ethyladenosine-3',5'-cyclic monophosphate, 2'-O-n-propyladenosine-3',5'-cyclic monophosphate,

2'-O-n-butyladenosine-3',5'-cyclic monophosphate, 2'-O-iso-butyladenosine-3',5'-cyclic monophosphate, 2'-O-methyladenosine-3',5'-cyclic monophosphate methyl triester and 2'-O-methyladenosine-3',5'-cyclic monophosphate phenyl triester).

ACTIVITY - Cytostatic; Antiinflammatory; Antidiabetic; Anticoagulant; Thrombolytic; Nootropic.

No biological data given.

MECHANISM OF ACTION - Exchange protein directly activated by **cAMP** (Epac) modulator; Epac-Rap1 signaling pathway modulator.

USE - The deoxyadenosine derivatives are useful in the manufacture of medicament for the **treatment** of human diseases e.g. cancer, chronic inflammation, thrombosis, type-2-diabetes mellitus (claimed) and mental disorder.

ADVANTAGE - The compounds modulate the activity of exchange proteins directly activated by **cAMP** (Epacs) and discriminate between Epac- and PKA-mediated signal transduction pathways. The compounds optionally are transformed into chemically labile prodrugs thus increasing lipophilicity and bioavailability.

Dwg.0/9

L19 ANSWER 9 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN DUPLICATE 7

ACCESSION NUMBER: 2003-712539 [67] WPIDS

DOC. NO. CPI: C2003-195914

TITLE: **Treating** animal following injury to area of central nervous system comprises administering cyclic nucleotide phosphodiesterase inhibitor and composition that increases intracellular levels of cyclic nucleotide cyclase, and implanting cells.

DERWENT CLASS: B05

INVENTOR(S): BUNGE, M B; PEARSE, D D

PATENT ASSIGNEE(S): (BUNG-I) BUNGE M B; (PEAR-I) PEARSE D D; (UYMI-N) UNIV MIAMI

COUNTRY COUNT: 103

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003065994	A2	20030814	(200367)*	EN	15
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2003220280	A1	20031127	(200378)		
AU 2003210869	A1	20030902	(200425)		
EP 1482916	A2	20041208	(200480)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
KR 2004101220	A	20041202	(200525)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003065994	A2	WO 2003-US3513	20030207
US 2003220280	A1 Provisional	US 2002-354306P	20020207
		US 2003-359554	20030207
AU 2003210869	A1	AU 2003-210869	20030207

EP 1482916	A2	EP 2003-737656	20030207
		WO 2003-US3513	20030207
KR 2004101220	A	KR 2004-712106	20040805

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003210869	A1 Based on	WO 2003065994
EP 1482916	A2 Based on	WO 2003065994

PRIORITY APPLN. INFO: US 2002-354306P 20020207; US 2003-359554 20030207

AB WO2003065994 A UPAB: 20031017
NOVELTY - **Treatment** (P1) of an animal following injury to an area of the central nervous system comprises:
(a) administering a cyclic nucleotide phosphodiesterase inhibitor (a1);
(b) administering a composition (C1) that elevates intracellular levels of a cyclic nucleotide cyclase, and
(c) implanting cells that provide or mimic the functions of neural cells native to the nervous system.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) **Treatment** (P1) of an animal following injury to an area of the central nervous system which comprises implanting Schwann cells at the site of injury, administering rolipram and administering dibutyryl **cyclic adenosine** monophosphate (db-**cAMP**), and
(2) a pharmaceutical composition (C2) which comprises a phosphodiesterase inhibitor and a compound (a2) that elevates intracellular levels of a cyclic nucleotide cyclase.
ACTIVITY - CNS-Gen.
MECHANISM OF ACTION - Phosphodiesterase inhibitor; Cyclic-Nucleotide-Cyclase-Agonist.
USE - Used for **treating** injury to an area of the central nervous system and to restore function after CNS injury (claimed).
ADVANTAGE - (P1) Improves motor and sensory function including consistent stepping, consistent coordination, correct foot placement and the ability to perform fine motor tasks in a similar fashion to the uninjured cells.
Dwg.0/7

L19 ANSWER 10 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-156325 [15] WPIDS
DOC. NO. NON-CPI: N2004-125175
DOC. NO. CPI: C2004-062002
TITLE: Fluorescent entity, useful as fluorescent tracer, comprises fluorophore and functional group, introduced or generated on the fluorophore or an oligonucleotide or oligonucleotide analog.
DERWENT CLASS: B04 D16 E13 E23 Q64
INVENTOR(S): BAZIN, H; MATHIS, G; MAURIN, F; TRINQUET, E
PATENT ASSIGNEE(S): (CISB-N) CIS BIO INT SA; (CISB-N) CIS BIO INT
COUNTRY COUNT: 104
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003104685	A2	20031218	(200415)*	EN	62

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL
PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU
ZA ZM ZW

FR 2840611 A1 20031212 (200415)
AU 2003242733 A1 20031222 (200445)
EP 1525211 A2 20050427 (200529) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
MC MK NL PT RO SE SI SK TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003104685	A2	WO 2003-EP6459	20030606
FR 2840611	A1	FR 2002-6948	20020606
AU 2003242733	A1	AU 2003-242733	20030606
EP 1525211	A2	EP 2003-757066	20030606
		WO 2003-EP6459	20030606

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003242733	A1 Based on	WO 2003104685
EP 1525211	A2 Based on	WO 2003104685

PRIORITY APPLN. INFO: FR 2002-6948 20020606

AB WO2003104685 A UPAB: 20040302

NOVELTY - A fluorescent entity (U) comprises: a fluorophore (except a rare earth metal cryptate); and at least one functional group, introduced or generated on the fluorophore or one of oligonucleotides or oligonucleotide analogs. The fluorophore is covalently attached to at least one oligonucleotide(s) or oligonucleotide analog(s).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) A fluorescent conjugate consisting of the entity covalently attached to a carrier molecule; and

(2) A method for increasing the fluorescence intensity of a fluorophore, for decreasing the aggregation at the surface or for increasing quantum yield of a fluorophore attached to a carrier molecule, in which a fluorescent entity is used as a fluorophore.

USE - The fluorescent entities (U) are useful as fluorescent tracer, for detecting and/or determining by fluorescence an analyte in a medium liable to contain it; for determining an interaction between biomolecules; or for determining a biological activity such as an enzyme activity, the activation of a membrane-bound receptor, the transcription of a gene, a membrane transport or a variation in membrane polarization; for screening medicinal products; as an acceptor fluorescent compound in the presence of a donor fluorescent compound; and as a donor fluorescent compound in the presence of an acceptor fluorescent compound. In fluorescence microscopy, in flow cytometry, in fluorescence polarization or in fluorescence correlation. To produce a conjugate. Also as a contrast agent for optical imaging in **vivo** (all claimed).

ADVANTAGE - The entities (U) makes it possible to produce conjugates exhibiting virtually zero aggregation of the fluorophore. The entity increases the quantum yield of a fluorophore attached to the carrier molecule. The conjugates are of great advantage in more conventional techniques of detection by fluorescence, where the number of fluorophores per carrier molecule, the quantum yield and the molar extinction

coefficient of the fluorophore are predominant criteria for the sensitivity of these systems.
Dwg.0/3

L19 ANSWER 11 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-381663 [36] WPIDS
DOC. NO. CPI: C2003-101414
TITLE: New antisense oligonucleotides for modulating CREB (**cAMP** response element binding protein) gene expression, useful for preventing or **treating** e.g. cancers, a disease arising from aberrant apoptosis, or neuronal disorders.
DERWENT CLASS: B04 D16
INVENTOR(S): COWSERT, L M; MONIA, B P
PATENT ASSIGNEE(S): (ISIS-N) ISIS PHARM INC; (COWS-I) COWSERT L M; (MONI-I) MONIA B P
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003030617	A2	20030417	(200336)*	EN	91
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW					
US 2003105038	A1	20030605	(200339)		
US 2004048825	A1	20040311	(200419)		
EP 1444366	A2	20040811	(200452)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
AU 2002362757	A1	20030422	(200460)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003030617	A2	WO 2002-US32181	20021007
US 2003105038	A1	US 2001-973827	20011010
US 2004048825	A1 Cont of	US 2001-973827	20011010
		US 2003-672981	20030926
EP 1444366	A2	EP 2002-800973	20021007
		WO 2002-US32181	20021007
AU 2002362757	A1	AU 2002-362757	20021007

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1444366	A2 Based on	WO 2003030617
AU 2002362757	A1 Based on	WO 2003030617

PRIORITY APPLN. INFO: US 2001-973827 20011010; US 2003-672981 20030926

AB WO2003030617 A UPAB: 20030609
NOVELTY - A compound that is 8-50 nucleobases in length, which:
(a) is targeted to a nucleic acid molecule encoding **cAMP** response element binding protein (CREB), and specifically hybridizes with

and inhibits the expression of CREB; or

(b) specifically hybridizes with at least an 8-nucleobase portion of an active site on a nucleic acid molecule encoding CREB, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) inhibiting the expression of CREB in cells or tissues comprising contacting the cells or tissues with the new compound, so that expression of CREB is inhibited; and

(2) a composition comprising the new compound and a pharmaceutical carrier or diluent.

ACTIVITY - Cytostatic; Neuroprotective.

Test details are described but no results are given.

MECHANISM OF ACTION - **cAMP** Response Element Binding Protein Inhibitor.

USE - The antisense oligonucleotide is useful for **treating** an animal having a disease or conditions associated with CREB, e.g. hyperproliferative disorder (particularly cancer), a disease or condition arising from aberrant apoptosis (claimed), or neuronal disorders. The antisense compounds are useful for diagnostics, **therapeutics**, prophylaxis, or as research reagents or kits. In particular, the antisense oligonucleotides are useful for preventing or delaying these conditions or disease.

Dwg.0/0

L19 ANSWER 12 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:749997 HCAPLUS

DOCUMENT NUMBER: 139:255334

TITLE: Compositions and methods using an RXR agonist and a protein kinase A activator for the treatment of hyperproliferative diseases

INVENTOR(S): Benoit, Gerard; Gronemeyer, Hinrich; Lanotte, Michel; Gottardis, Marco

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; Institut National de la Sante et de la Recherche Medicale; Centre National de la Recherche Scientifique; Universite Louis Pasteur

SOURCE: U.S., 35 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6624154	B1	20030923	US 2000-556675		20000421
PRIORITY APPLN. INFO.:			US 1999-130649P	P	19990423

OTHER SOURCE(S): MARPAT 139:255334

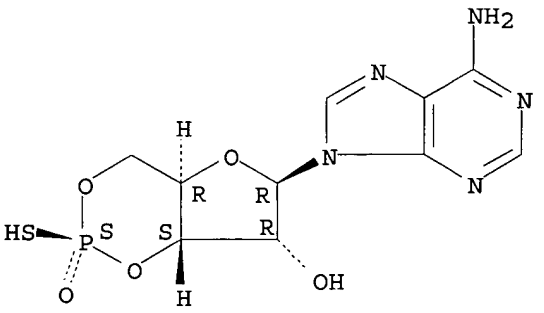
AB The invention discloses compns. comprising a retinoid X receptor agonist and an agent capable of activating protein kinase A. The invention also discloses methods for treating hyperproliferative diseases (e.g. leukemia, breast cancer) by administering a retinoid X receptor agonist and an agent capable of activating protein kinase A. Prepn of 4-[1-(5,6-dihydro-3,5,5-trimethyl-8-isopropyl-2-naphthalenyl)ethenyl] benzoic acid is described.

IT **71774-13-5**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(RXR agonist and protein kinase A activator for treatment of hyperproliferative diseases, and use with other agents)

RN 71774-13-5 HCAPLUS

CN Adenosine, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 108 THERE ARE 108 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 13 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:513468 HCAPLUS
DOCUMENT NUMBER: 139:332591
TITLE: Synergistic antiproliferative and apoptotic effects induced by epidermal growth factor receptor and protein kinase A inhibitors in human prostatic cancer cell lines
AUTHOR(S): Mimeault, Murielle; Pommery, Nicole; Henichart, Jean-Pierre
CORPORATE SOURCE: Institut de Chimie Pharmaceutique Albert Lespagnol, Lille, Fr.
SOURCE: International Journal of Cancer (2003), 106(1), 116-124
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Our results revealed that the blockade of epidermal growth factor receptor (EGFR) tyrosine kinase and protein kinase A (PKA) signaling pathways by specific inhibitors (PD153035 and Rp-cAMPs) leads to a synergistic inhibition of EGF- and serum-stimulated growth of human prostatic cancer cells (LNCaP, DU145 and PC3) concomitant with an arrest in the G1 phase of cellular cycle. Of particular interest, the combination of PD153035 and Rp-cAMPs also caused a more substantial apoptotic/necrotic death of these prostatic cancer cells as compared to drugs alone. Moreover, we observed that the inhibition of acidic sphingomyelinase and caspase cascades results in a marked reduction of DNA fragmentation and apoptotic death induced by PD153035, alone or in combination with Rp-cAMPs, in EGF stimulated PC3 cells. This suggests that these agents might mediate their cytotoxic effects at least in part vla the ceramide generation and activation of caspase signaling pathways. N-oleoylethanolamine (OE), an inhibitor of acidic ceramidase, consistently potentiated the apoptotic effects of PD153035 in all the prostatic cancer cell lines tested. Addnl., the cellular ceramide content estimated for PC3 cells was increased after treatment with PD153035, alone or in combination, at a lower dose with OE and Rp-cAMPs. The synergistic apoptotic effect of PD153035 plus Rp-cAMPs induced in PC3 was also accompanied by a significant rate of mitochondrial membrane depolarization and release of cytochrome c into cytosol as

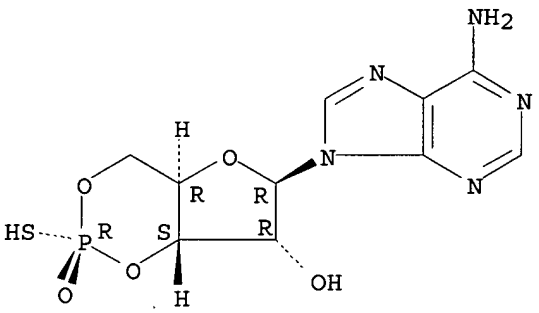
compared to drugs alone. Combined, the results indicated that the simultaneous inhibition of EGFR and PKA signaling cascades might lead to a more massive apoptotic death of metastatic prostatic cancer cells by increasing ceramide accumulation and activating of caspase cascade of a mitochondrial dependent manner.

IT **73208-40-9**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(synergistic antiproliferative and apoptotic mechanism induced by EGFRTK and PKA inhibitors in human prostatic cancer cell lines)

RN 73208-40-9 HCAPLUS

CN Adenosine, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 14 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:946447 HCAPLUS
DOCUMENT NUMBER: 138:23656
TITLE: Modulating neuronal outgrowth via the major histocompatibility complex class I (MHC I) molecule
INVENTOR(S): Kaufman, Daniel L.; Hanssen, Lorraine; Zekzer, Daniel
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002099069	A2	20021212	WO 2002-US17743	20020605
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003049254	A1	20030313	US 2002-161647	20020605

PRIORITY APPLN. INFO.: US 2001-295596P P 20010605

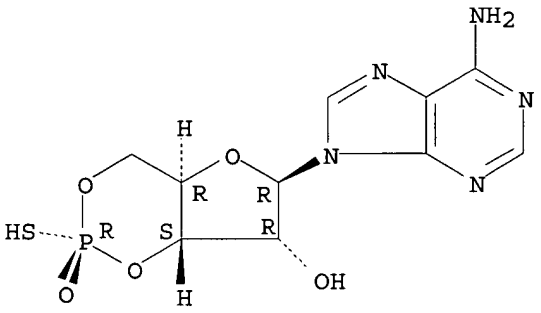
AB The invention relates to methods and compns. for treating neural damage caused by injury or disease, by enhancing neural outgrowth and/or repair responses in the nervous system. Preferably, the methods and compns. utilize agents which interfere with the ability of the major histocompatibility complex (MHC) class I mol. (MHC I) to inhibit neurite outgrowth. Such agents include antibodies directed to MHC I, MHC I fragments and/or analogs, and agents which interfere with MHC I interaction with its neuronal receptor and the receptor's signaling pathway.

IT **73208-40-9**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(modulation of neuronal outgrowth via the major histocompatibility complex class I mols.)

RN 73208-40-9 HCAPLUS

CN Adenosine, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 15 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:91515 HCAPLUS

DOCUMENT NUMBER: 134:141756

TITLE: Compositions and methods using cyclic AMP formation- or ion channel-associated receptor antagonists for the treatment of neurological disorders and neurodegenerative diseases

INVENTOR(S): Lee, Robert K. K.; Wurtman, Richard J.

PATENT ASSIGNEE(S): USA

SOURCE: U.S., 46 pp., Cont.-in-part of U.S. 6,043,224.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6184248	B1	20010206	US 1999-435470	19991108
US 6187756	B1	20010213	US 2000-493228	20000128
CA 2390655	AA	20010517	CA 2000-2390655	20001108
WO 2001034138	A1	20010517	WO 2000-US30663	20001108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1242063	A1	20020925	EP 2000-977048	20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003513917	T2	20030415	JP 2001-536138	20001108
US 2002052407	A1	20020502	US 2001-775809	20010205
US 6469055	B2	20021022		

PRIORITY APPLN. INFO.:	US 1996-25507P	P	19960905
	US 1997-33765P	P	19970115
	US 1997-924505	A2	19970905
	US 1999-435470	A	19991108
	WO 2000-US30663	W	20001108

AB It has been discovered that the stimulation of β-adrenergic receptors, which activate cAMP formation, give rise to increased amyloid precursor protein (APP) and glial fibrillary acidic protein (GFAP) synthesis in astrocytes. Hence, the in vitro or in vivo exposure of neuronal cells to certain compns. comprising β-adrenergic receptor ligands or agonists, including e.g., norepinephrine, isoproterenol and the like, increases APP mRNA transcription and consequent APP overprodn. These increases are blocked by β-adrenergic receptor antagonists, e.g. propranolol. The in vitro or in vivo treatment of these cells with 8-Br-cAMP, prostaglandin E2 (PGE2), forskolin, and nicotine ditartrate also increased APP synthesis, including an increase in mRNA and holoprotein levels, as well as an increase in the expression of GFAP. Compns. and methods are disclosed of regulating APP overexpression and mediating reactive astrogliosis through cAMP signaling or the activation of β-adrenergic receptors. It has further been found that the increase in APP synthesis caused by 8-Br-cAMP, PGE2, or forskolin is inhibited by immunosuppressants, immunophilin ligands, or antiinflammatory agents, e.g. cyclosporin A and FK-506 (tacrolimus), as well as ion-channel modulators, including ion chelating agents, e.g. EGTA, or calcium/calmodulin kinase inhibitors, e.g. KN93. The invention has broad implications in the alleviation, treatment, or prevention of neurol. disorders and neurodegenerative diseases, including Alzheimer's Disease.

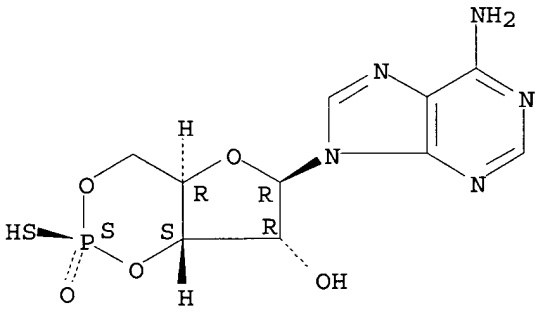
IT **93602-66-5**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(cAMP formation- or ion channel-associated receptor antagonists for treatment of neurol. disorders and neurodegenerative diseases)

RN 93602-66-5 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen (S)-phosphorothioate], compd. with N,N-diethylethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

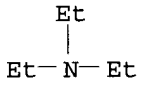
CRN 71774-13-5
CMF C10 H12 N5 O5 P S

Absolute stereochemistry.



CM 2

CRN 121-44-8
CMF C6 H15 N



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 16 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:93872 HCAPLUS
DOCUMENT NUMBER: 134:157586
TITLE: Use of substances increasing the intracellular content of cyclic AMP or stimulating activity of cyclic AMP binding proteins for the treatment of illnesses of the bladder
INVENTOR(S): Truss, Michael Carsten; Stief, Christian G.; Jonas, Udo; Uckert, Stefan; Becker, Armin J.; Forssmann, Wolf-Georg
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19935209	A1	20010208	DE 1999-19935209	19990727
PRIORITY APPLN. INFO.:			DE 1999-19935209	19990727

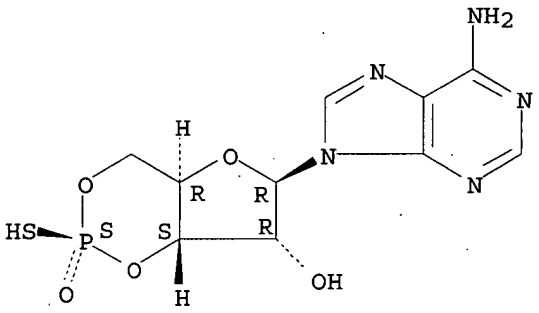
AB The invention discloses the use of substances increasing the intracellular concentration of cAMP by direct stimulation of adenyl cyclase activity, associating with β receptors, or inhibiting cAMP-hydrolyzing phosphodiesterases 1, 2, 3, 4, 7, or 8, or stimulate the functional activity of cAMP binding proteins, for the treatment of urinary bladder storage function disturbances (urge symptomatol., urge incontinence, pollakiuria, Nycturia, and detrusor muscle instability). Such substances include e.g. forskolin, L-858051, adenyl cyclase toxin, xamoterol, denopamine, clenbuterol,

procaterol, salbutamol, sameterol, formoterol, terbutaline, fenoterol, BRL 37344, ZD 7114, CPG 12177, CL 316243, ICI 215.001, pindolol, IBMX, methoxymethyl-IBMX, vinpocetin, vincamin, HA-588, calmodulin antagonists, EHNA, amrinone, OPC 3698, enoximone, milrinone, Ro 13-6438, siguazodan, HL 725, 8-Br-cGMP, 8-pCPT-cGMP, Sp-8-Br-cGMPS, PET GCMcP, CD-80.633, BRL 30892, SQ 20009, 3-ethyl-1-(4-fluorophenyl)-6-phenyl-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolopyridine, ZK 62711, Ro 20-1724,, RP 73401, RS 25344, SB 2074499, TVX 2706, zardaverine, 8-bromo-cAMP, and Sp-cAMPS.

IT **71774-13-5 142754-28-7**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(substances increasing the intracellular content of cAMP or stimulating activity of cAMP binding proteins for the treatment of illnesses of the bladder)

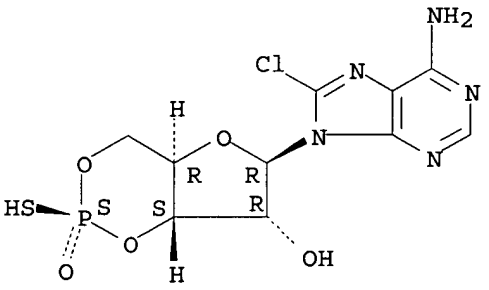
RN 71774-13-5 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 142754-28-7 HCAPLUS
CN Adenosine, 8-chloro-, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

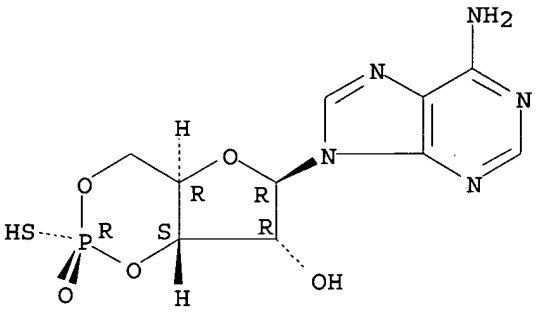


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 17 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:93273 HCAPLUS
DOCUMENT NUMBER: 134:336188
TITLE: Mechanisms of hydrogen peroxide-induced relaxation in rabbit mesenteric small artery

AUTHOR(S): Fujimoto, S.; Asano, T.; Sakai, M.; Sakurai, K.; Takagi, D.; Yoshimoto, N.; Itoh, T.
CORPORATE SOURCE: Department of Pharmacology, Nagoya City University Medical School, Kawasumi, Mizuho-ku, Nagoya, 467-8601, Japan
SOURCE: European Journal of Pharmacology (2001), 412(3), 291-300
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of hydrogen peroxide were studied on isolated rabbit mesenteric small artery; rabbit superior mesenteric artery and mouse aorta were also studied as reference tissues. For mesenteric small artery, hydrogen peroxide (1 to 100 μM) relaxed a norepinephrine-stimulated artery in a concentration-dependent manner. The relaxation was not significantly affected by removal of the endothelium and was less pronounced in arteries contracted with high-KCl solution plus norepinephrine than in those contracted with norepinephrine alone. The relaxation response to hydrogen peroxide was increased by isobutylmethylxanthine and zaprinast, inhibited by diclofenac, methylene blue and dithiothreitol and unaffected by atropine, tetraethylammonium, superoxide dismutase, deferoxamine, DMSO or the Rp stereoisomer of adenosine cyclic monophosphothioate. Hydrogen peroxide shifted concentration-contractile response curves for norepinephrine to the right and downwards. Norepinephrine and caffeine elicited a transient, phasic contraction of the mesenteric small artery exposed for 0.5, 1 and 2 min to a Ca2+-free solution Hydrogen peroxide inhibited the norepinephrine-induced contraction, and to a lesser extent the caffeine-induced contraction, and verapamil did not alter the contraction to norepinephrine. These pharmacol. properties of hydrogen peroxide were similar to those of 8-bromo cGMP; 8-bromo cGMP inhibited more potently the norepinephrine-induced than the KCl-induced contraction and the contraction elicited by norepinephrine in Ca2+-free solution The present results suggest that hydrogen peroxide induces endothelium-independent relaxation of the rabbit mesenteric small artery precontracted with norepinephrine. The effects of hydrogen peroxide may be at least in part mediated by cGMP and cyclooxygenase products in the vascular smooth muscles now used.
IT **73208-40-9**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(mechanisms of hydrogen peroxide-induced relaxation in mesenteric small artery)
RN 73208-40-9 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 18 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:772398 HCAPLUS
DOCUMENT NUMBER: 133:344604
TITLE: Compositions and methods using a retinoid X receptor agonist and a protein kinase A activator for treatment of hyperproliferative diseases
INVENTOR(S): Benoit, Gerard; Gronemeyer, Hinrich; Lanotte, Michel; Gottardis, Marco
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; Institut National de la Sante et de la Recherche Medicale; Centre National de la Recherche Scientifique; Universite Louis Pasteur
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

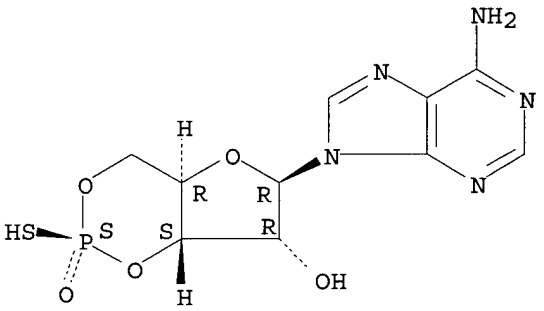
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064260	A1	20001102	WO 1999-US8908	19990423
W: AU, CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2369910	AA	20001102	CA 1999-2369910	19990423
AU 9941815	A1	20001110	AU 1999-41815	19990423
AU 773928	B2	20040610		
EP 1173061	A1	20020123	EP 1999-925558	19990423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002542268	T2	20021210	JP 2000-613263	19990423
PRIORITY APPLN. INFO.:			WO 1999-US8908 W	19990423

AB The invention provides compns. comprising a retinoid X receptor agonist and an agent capable of activating protein kinase A. The invention also provides methods of treating hyperproliferative diseases by administering a retinoid X receptor agonist and an agent capable of activating protein kinase A.

IT **71774-13-5**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(retinoid X receptor agonist and protein kinase A activator for

treatment of hyperproliferative disease)
RN 71774-13-5 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 19 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:161140 HCAPLUS
DOCUMENT NUMBER: 132:203156
TITLE: Cyclic nucleotide-dependent protein kinase activators for promoters of neural regeneration
INVENTOR(S): Song, Hongjun; Poo, Mu-ming; Ming, Guo-li; Tessier-Lavigne, Marc; He, Zhigang
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012099	A1	20000309	WO 1999-US20139	19990902
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6268352	B1	20010731	US 1998-145820	19980902
CA 2342350	AA	20000309	CA 1999-2342350	19990902
AU 9957033	A1	20000321	AU 1999-57033	19990902
EP 1109561	A1	20010627	EP 1999-944061	19990902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002523462	T2	20020730	JP 2000-567216	19990902
US 2002006916	A1	20020117	US 2001-900268	20010706
US 6512004	B2	20030128		
US 2002142990	A1	20021003	US 2002-90095	20020228

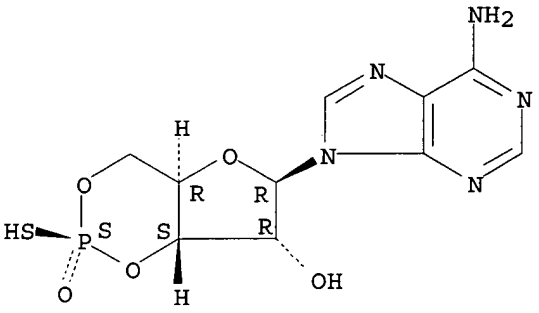
US 2003134820	A1	20030717	US 2002-272741	20021017
US 2003134821	A1	20030717	US 2002-272774	20021017
PRIORITY APPLN. INFO.:			US 1998-145820	A 19980902
			WO 1999-US20139	W 19990902
			US 2001-900268	A1 20010706

AB Methods and compns. are provided for promoting neural cell growth and/or regeneration. The general methods involve contacting with an activator of a cyclic nucleotide-dependent protein kinase a neural cell subject to growth repulsion mediated by a neural cell growth repulsion factor. The activator may comprise a direct or an indirect activator of the protein kinase; the repulsion factor typically comprises one or more natural, endogenous proteins mediating localized repulsion or inhibition of neural cell growth; and the target cells are generally vertebrate neurons, typically injured mammalian neurons. The subject compns. include mixts. comprising a neural cell, an activator of a cyclic nucleotide-dependent protein kinase, and a neural cell growth repulsion factor.

IT **71774-13-5 73208-40-9 127634-20-2**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclic nucleotide-dependent protein kinase activators for promoters of neural regeneration)

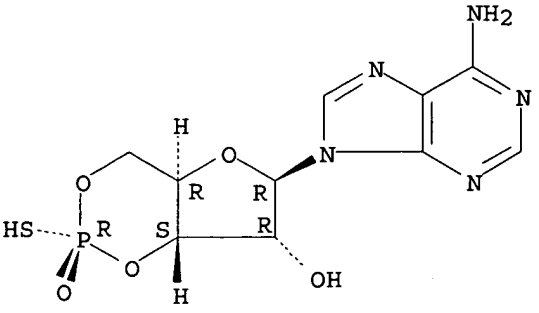
RN 71774-13-5 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



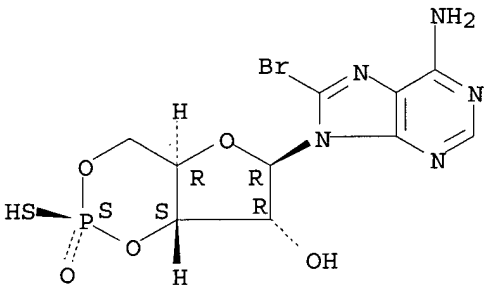
RN 73208-40-9 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 127634-20-2 HCAPLUS
CN Adenosine, 8-bromo-, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 20 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:663185 HCAPLUS
DOCUMENT NUMBER: 134:157447
TITLE: Conditioned locomotion in rats following amphetamine infusion into the nucleus accumbens: blockade by coincident inhibition of protein kinase A
AUTHOR(S): Sutton, M. A.; McGibney, K.; Beninger, R. J.
CORPORATE SOURCE: Department of Psychology, Queen's University, Kingston, ON, K7L 3N6, Can.
SOURCE: Behavioural Pharmacology (2000), 11(5), 365-376
CODEN: BPHAEL; ISSN: 0955-8810
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of protein kinase A (PKA) inhibition on the unconditioned and conditioned locomotor-activating properties of amphetamine injection into the nucleus accumbens was determined Rats underwent three 60-min conditioning sessions, pairing a test environment with bilateral coinfusions of amphetamine (25 μg/side) and the PKA inhibitor Rp-adenosine 3',5'-cyclic monophosphothioate triethylamine (Rp-cAMPS) (0, 2.5, 250, 500 ng, 1, 10 or 20 μg/side). Two addnl. groups (receiving amphetamine explicitly unpaired with the environment or saline/environment pairings) served as controls. In a subsequent drug-free 60-min session, the animals that had received amphetamine/environment pairings demonstrated conditioned locomotion relative to controls. Rp-cAMPS cotreatment during pairing sessions differentially affected conditioned and unconditioned locomotor activation. Amphetamine-induced unconditioned activity was enhanced by 500 ng and 1 μg Rp-cAMPS, locomotor sensitization was enhanced by 250 ng-1 μg Rp-cAMPS, and conditioned activity was attenuated by 1 μg Rp-cAMPS and blocked by 10 and 20 μg Rp-cAMPS. Thus, unconditioned activity and locomotor sensitization were enhanced at doses (250 ng-1 μg) that either did not affect or attenuated conditioned activity, while conditioned activity was reduced or blocked at doses (1-20 μg) that enhanced or did not affect overall unconditioned activity. These results demonstrate that the activation of PKA plays a critical role in the process by which properties of drugs become associated with environmental stimuli.

IT **151837-09-1**

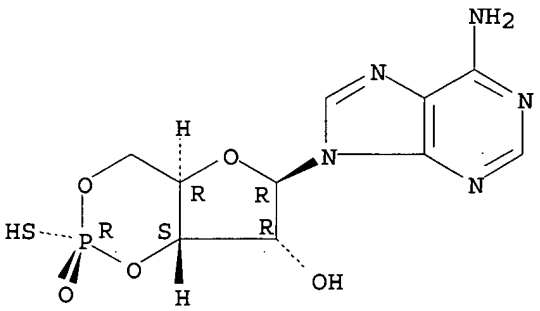
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(protein kinase A inhibition by Rp-cAMPS effect on conditioned locomotion in rats following amphetamine infusion into the nucleus accumbens)

RN 151837-09-1 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen (R)-phosphorothioate], compd. with N,N-diethylethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

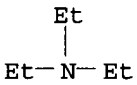
CRN 73208-40-9
CMF C10 H12 N5 O5 P S

Absolute stereochemistry.



CM 2

CRN 121-44-8
CMF C6 H15 N



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 21 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-527403 [44] WPIDS
DOC. NO. CPI: C1999-154905
TITLE: Modulating the negative effects of mutations of the MEC1 gene such as neurological defects.
DERWENT CLASS: B04 D16
INVENTOR(S): GAZAWAY, B K; PEETERS, H W; STRAWN, R; VOLK, M; VON DEN NIEUWELAAR, A J; CROSS, F R; VALLEN, E A
PATENT ASSIGNEE(S): (HUTC-N) HUTCHINSON CANCER RES CENT FRED; (STRK) STORK GAMCO INC
COUNTRY COUNT: 81
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9941984	A1	19990826	(199944)*	EN	31

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE GH
GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MD MG MK
MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ
VN YU ZW

AU 9929720	A	19990906 (200003)
US 6383069	B1	20020507 (200235)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9941984	A1	WO 1999-US3702	19990219
AU 9929720	A	AU 1999-29720	19990219
US 6383069	B1 Provisional	US 1998-75342P	19980220
	Div ex	US 1998-115845	19980715
		US 2000-519914	20000307

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9929720	A Based on	WO 9941984
US 6383069	B1 Div ex	US 6190250

PRIORITY APPLN. INFO: US 1998-75342P 19980220; US
1998-115845 19980715; US
2000-519914 20000307

AB WO 9941984 A UPAB: 20011203
NOVELTY - Arresting, alleviating, **treating**, counteracting, reversing, or preventing the negative effects of an undesirable mutation in the MEC1 gene or its homolog, which mutation is harbored by a eukaryote, comprises increasing the amount of ribonucleotide reductase (RNR) protein in the eukaryote.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of inhibiting or arresting the growth of or inducing cell death in a cell, which is over-expressing cyclin or cyclin-like protein, comprising contacting the cell with a growth inhibiting, growth arresting, or cell death inducing amount of an agent that inhibits the activity of phosphoinositide kinase (PIK) or PIK-related kinase.

USE - The negative effects of the MEC1 mutation include neurological defects, cerebellar degeneration, immune deficiency, premature aging, an increased risk of developing cancer, sensitivity to radiation, dilation of blood vessels, or progressive mental retardation (all claimed).

ADVANTAGE - None given.

Dwg.0/5

L19 ANSWER 22 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-347612 [29] WPIDS
DOC. NO. CPI: C1999-102323
TITLE: Nucleic acids that compete with response elements' for transcription factors.
DERWENT CLASS: B04 D16
INVENTOR(S): CHO-CHUNG, Y S
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 77
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

```
-----------------------------------------------
WO 9926634      A1 19990603 (199929)* EN   83
   RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
       OA PT SD SE SZ UG ZW
    W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GD GE HU
       IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ
       PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9916098      A  19990615 (199944)
US 6060310      A  20000509 (200030)
EP 1037641      A1 20000927 (200048)  EN
    R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
       RO SE SI
AU 746791       B  20020502 (200238)
CA 2311182      C  20040330 (200424)  EN
```

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9926634	A1	WO 1998-US25307	19981123
AU 9916098	A	AU 1999-16098	19981123
US 6060310	A	US 1997-977643	19971124
EP 1037641	A1	EP 1998-960516	19981123
		WO 1998-US25307	19981123
AU 746791	B	AU 1999-16098	19981123
CA 2311182	C	CA 1998-2311182	19981123
		WO 1998-US25307	19981123

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9916098	A	Based on	WO 9926634
EP 1037641	A1	Based on	WO 9926634
AU 746791	B	Previous Publ.	AU 9916098
		Based on	WO 9926634
CA 2311182	C	Based on	WO 9926634

PRIORITY APPLN. INFO: US 1997-977643 19971124

AB WO 9926634 A UPAB: 19990723

NOVELTY - Composition (A) comprises one or more nucleic acids (I) that compete with **cAMP** (**cyclic adenosine** monophosphate) response element (CRE) enhancer DNA for binding to transcription factors (TF).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) method for regulating gene transcription in target cells, which contain CRE-enhancer DNA and TF that associates with this DNA, by **treating** the cells with CRE decoys, i.e. (I), so that this competes with the DNA for binding to TF; and

(2) the method of (a) for regulating cancer cell proliferation in **vivo.**

ACTIVITY - Anticancer; antiviral.

MECHANISM OF ACTION - (I) alter gene expression by competing for TF, preventing this from binding to native response elements. They induce cell differentiation or apoptosis, and inhibit both basal and **cAMP** -induced expression of CRE-containing genes, including those for **cAMP**-dependent protein kinase and phosphoenol pyruvate carboxykinase. (I) also induce production of the kinase inhibitor p21Cip1/WAF1 and increase expression or activity of p53.

USE - (I) are used to regulate gene transcription in cells, in vitro or in **vivo**, specifically for inhibiting proliferation of cancer cells, but possibly also for regulation of metabolism in hepatitis B and other viruses. HCT-15 human multidrug resistant colon carcinoma cells (2 million) were inoculated subcutaneously into the flank of nude mice, then the CRE oligonucleotide 5'-TGACGTTCATGACGTTCATGACGTTCA-3' injected intraperitoneally at doses of 0.1 mg, 5 times per week, once the tumor had reached 30-50 mg. This **treatment** resulted in over 85% reduction in tumor growth, relative to an untreated control.

ADVANTAGE - (I) have high affinity for TF and can inhibit growth of cancer cells without adverse effects on normal cells (contrast use of antisense RNA). The method does not require knowledge of the target gene sequence, only of the response element sequence.

Dwg.0/13

L19 ANSWER 23 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-228548 [19] WPIDS
DOC. NO. CPI: C1999-067199
TITLE: Antisense oligodeoxynucleotides specific for mRNA encoding phosphodiesterase PDE1B1 enzymes and method for using them to induce apoptosis of cells - useful in the **treatment** of immunoproliferative disorders and immune disfunctions.
DERWENT CLASS: B04 D16
INVENTOR(S): EPSTEIN, P M
PATENT ASSIGNEE(S): (EPST-I) EPSTEIN P M
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5885834	A	19990323	(199919)*	EN	35

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5885834	A Provisional	US 1996-27207P	19960930
		US 1997-940332	19970930

PRIORITY APPLN. INFO: US 1996-27207P 19960930; US 1997-940332 19970930

AB US 5885834 A UPAB: 19990518

NOVELTY - Antisense oligodeoxynucleotides (AS-ODN(s)) which will bind to mRNA encoding phosphodiesterase PDE1B1 enzymes and their use in inducing programmed cell death (apoptosis) in cancer cells, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for: (i) a method (X) of inducing programmed cell death in cancer cells which comprises: (1) identifying the phosphodiesterase enzyme PDE1B1 in a cell line containing the cancer cells; (2) synthesising an AS-ODN inhibitor which will bind to mRNA encoding PDE1B1; and (3) applying the AS-ODN to the cell line to inhibit the enzymatic activity of the PDE1B1 and induce apoptosis in the cells; (ii) a purified and isolated polynucleotide (I) encoding a 63 kDa calmodulin-dependent phosphodiesterase PDE1B1 enzyme from a human leukemic lymphoblastoid cell line; and (iii) an AS-ODN (asI) which will bind to mRNA encoding phosphodiesterase PDE1B1 enzymes.

ACTIVITY - Cytostatic; Apoptotic

MECHANISM OF ACTION - AS-ODNs inhibit the expression of a protein by two mechanisms: (i) by degradation of RNA by the ubiquitous enzyme RNase

H, which selectively cleaves the RNA of DNA-RNA heteroduplexes; and (ii) the arrest of translation initiation caused by AS-ODN hybridization to the 5' un-translated region or the translation initiation site on the mRNA. Inhibition of phosphodiesterase (PDE) enzyme expression results in elevated levels of **cAMP** in the cells due to PDE1B1 being involved in the metabolism of **cAMP**. The elevated **cAMP** levels result in apoptosis by inhibition of DNA synthesis.

RPMI 8392 cells were studied for the presence of PDE1B1 mRNA using quantitive Reverse Transcription Polymerase Chain Reaction (RT-PCR) with primers specific for PDE1B1 DNA. It was found that the level PDE1B1 mRNA was diminished after 1 day in cells **treated** with 10-30 mu M AS-ODN, and undetectable after 2 days. Experiments were conducted to determine if inhibition of the expression of the gene for PDE1B1 could induce apoptosis. Based on the nucleotide (nt) sequence obtained for PDE1B1 from RPMI 8392 cells, an 18 nt **phosphorothioate** antisense oligodeoxynucleotide (PS-ODN) was synthesized starting from 6 nt to the 5'-end of the translation initiation codon and extending over the first 4 codons of the Open Reading Frame (ORF). As a control, a nonsense oligodeoxynucleotide (NS-ODN) containing the same base composition, but in a random, scrambled order, was also synthesized. These synthetic **phosphorothioate** ODNs were added to RPMI 8392 cells in concentrations from 0.3-30 mM and the cells were examined for apoptosis. DNA isolated from RPAR 8392 cells was analyzed for fragmentation on 2% agarose gels after the cells were cultured with different concentrations of **phosphorothioate** antisense (AS) or **phosphorothioate** nonsense (NS) ODN for 2 days or 1, 2 and 3 days. Cell culture was done at a concentration of about 106/ml in 1 ml volumes in 24 well plates, in RPMI 1640 growth medium-L except that the fetal calf serum was heat inactivated at 65 0C for 1 hour (hr) to help minimize nuclease activity. The sequence of the 18 nt AS-ODN used was 5'-GGACAGCFCCATGCTCAG-3', and the sequence of the 18 nt NS-ODN used was 5'-TACGTGAGGCACCTACGC-3'. Controls (lane 2 in all gels) represent no additions of ODN to the cells. Markers (lane 1 in all gels) are Hae III digests of fX174 DNA from GIIBCO/BRL. 48 hr **treatment** with 30 mM AS-ODN clearly induced apoptosis in these cells, whereas 30 mM NS-ODN did not. When cells were examined for apoptosis at 1, 2. and 3 days after addition of AS and NS-ODNS, it was found that after 3 days, AS-ODN induced apoptosis at both 10 mM and 30 mM, whereas in all cases, NS-ODN had no effect.

USE - The method (X) and AS-ODN (asI) are useful in inducing **cAMP** stimulated apoptosis and may be in the **treatment** of immunoproliferative disorders and immune disfunctions such as acute lympholytic leukemia, breast and prostate cancer.

ADVANTAGE - It is known that increasing cellular **cAMP** levels can lead to cell death and the use of **cAMP** analogues or agents which increase **cAMP** content has been suggested as a method of **treating** cancers by inducing apoptosis. However **cAMP** has profound side effects on the metabolic machinery, growth regulation and transcription in most cells. Indiscriminate elevation of **cAMP** throughout the body would probably produce a wide range of side effects. The antisense oligodeoxynucleotide (AS-ODN) (asI) is capable of selectively inhibiting the expression of a specific isoform of the PDE enzyme (PDE1B1) to cause an increase in the cell **cAMP** content and apoptosis in cancer tissue. (asI) is selective because PDE1B1 is only expressed in cancerous cells, therefore the use of (I) avoids the adverse effect associated with a systemic increase in **cAMP** levels. In particular, the use of AS-ODNs is unlikely to affect brain function as AS-ODNs distribute poorly into the brain tissue.

Dwg.0/0

L19 ANSWER 24 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:184143 HCAPLUS
DOCUMENT NUMBER: 130:218318
TITLE: Use of purine nucleosides for modulating the axonal outgrowth of central nervous system neurons
INVENTOR(S): Benowitz, Larry I.
PATENT ASSIGNEE(S): Children's Medical Center Corporation, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911274	A1	19990311	WO 1998-US3001	19980220
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6440455	B1	20020827	US 1997-921902	19970902
CA 2302156	AA	19990311	CA 1998-2302156	19980220
AU 9866568	A1	19990322	AU 1998-66568	19980220
AU 748961	B2	20020613		
EP 1009412	A1	20000621	EP 1998-908565	19980220
EP 1009412	B1	20040728		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001516695	T2	20011002	JP 2000-508376	19980220
NZ 503073	A	20021126	NZ 1998-503073	19980220
RU 2212241	C2	20030920	RU 2000-108443	19980220
AT 271874	E	20040815	AT 1998-908565	19980220
EP 1466606	A2	20041013	EP 2004-9962	19980220
EP 1466606	A3	20041124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2002042390	A1	20020411	US 2001-997688	20011129
US 6551612	B2	20030422		
US 2002055484	A1	20020509	US 2001-997687	20011129
US 2002128223	A1	20020912	US 2002-145224	20020514
US 2002137721	A1	20020926	US 2002-144952	20020514
US 2004014710	A1	20040122	US 2003-385031	20030310

PRIORITY APPLN. INFO.:

US 1997-921902	A2	19970902
EP 1998-908565	A3	19980220
WO 1998-US3001	W	19980220
US 2001-997687	B1	20011129

AB Methods and compns. for modulating the axonal outgrowth of central nervous system neurons are provided. Methods for stimulating the axonal outgrowth of central nervous system neurons following an injury (e.g., stroke, Traumatic Brain Injury, cerebral aneurism, spinal cord injury and the like) and methods for inhibiting the axonal outgrowth of central nervous system neurons in conditions such as epilepsy, e.g., post-traumatic epilepsy, and neuropathic pain syndrome, are also provided. These methods generally involve contacting the central nervous system neurons with a purine nucleoside, or analog thereof. Preferably, inosine or guanosine is used to stimulate axonal outgrowth and 6-thioguanine is used to inhibit

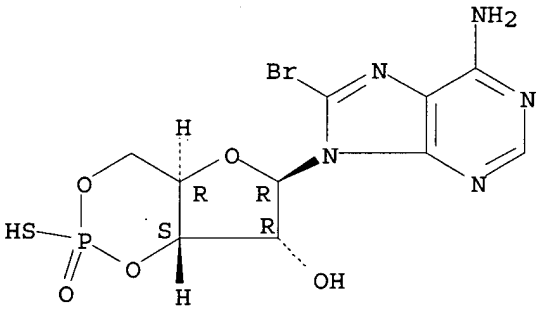
axonal outgrowth. The methods and compns. are particularly useful for modulating the axonal outgrowth of mammalian central nervous system neurons, such as mammalian retinal ganglion cells. Pharmaceutical and packaged formulations that include the purine nucleosides, and analogs thereof, of the invention are also provided.

IT **152322-58-2**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)

RN 152322-58-2 HCAPLUS

CN Adenosine, 8-bromo-, cyclic 3',5'-(hydrogen phosphorothioate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 25 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:670111 HCAPLUS
DOCUMENT NUMBER: 131:281568
TITLE: Method using a cAMP or cGMP analog, a phosphodiesterase inhibitor, or a nitric oxide precursor, donor, or analog for inducing vasorelaxation to treat pulmonary hypertension
INVENTOR(S): Lawson, Charles A.; Pinsky, David J.; Smerling, Arthur; Stern, David M.
PATENT ASSIGNEE(S): The Trustees of Columbia University In the City of New York, USA
SOURCE: U.S., 47 pp., Cont.-in-part of U. S. Ser. No.131,984.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5968911	A	19991019	US 1997-362571	19970218
US 5728705	A	19980317	US 1993-131984	19931004
WO 9509636	A1	19950413	WO 1994-US11248	19941004
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: US 1993-131984 A2 19931004
WO 1994-US11248 W 19941004

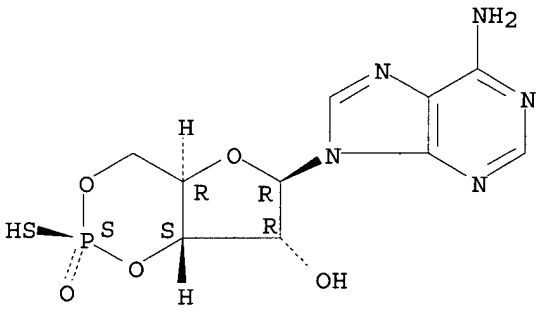
AB A method is provided for selectively decreasing pulmonary vascular resistance in a subject by administering endobronchially a drug chosen from among cAMP analogs, cGMP analogs, phosphodiesterase inhibitors, nitric oxide precursors, nitric oxide donors, and nitric oxide analogs.

IT **71774-13-5**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cAMP or cGMP analog, phosphodiesterase inhibitor, or nitric oxide precursor, donor, or analog for inducing vasorelaxation to treat pulmonary hypertension)

RN 71774-13-5 HCAPLUS

CN Adenosine, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 26 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:22669 HCAPLUS

DOCUMENT NUMBER: 132:333178

TITLE: Additive effects of IL-2 and protein kinase A type I antagonist on function of T cells from HIV-infected patients on HAART

AUTHOR(S): Aandahl, Einar Martin; Aukrust, Pal; Muller, Fredrik; Hansson, Vidar; Tasken, Kjetil; Froland, Stig S.

CORPORATE SOURCE: Institute of Medical Biochemistry, University of Oslo, Oslo, N-0317, Norway

SOURCE: AIDS (London) (1999), 13(17), F109-F114
CODEN: AIDSET; ISSN: 0269-9370

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

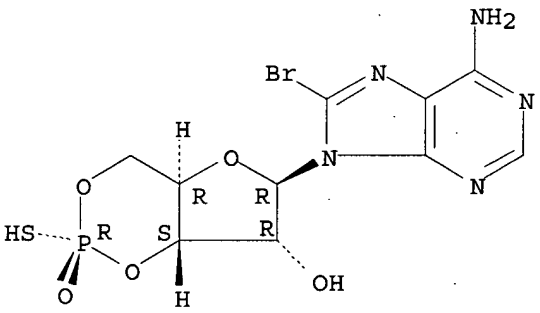
AB The objective was to explore the basis for a possible immunomodulatory combination therapy with IL-2 and agents inhibiting protein kinase A (PKA) type I. Highly active antiretroviral therapy (HAART) has dramatically improved HIV therapy, but fails to eradicate the virus, and the persistence of HIV-associated immunodeficiency demonstrates the need for addnl. immunomodulating therapies. The authors have previously shown that hyperactivation of PKA type I inhibits the function of HIV-infected patient T cells. The sep. and combined effect of a PKA type I-selective antagonist (Rp-8-Br-cAMPS) and interleukin (IL)-2 on the function of T cells from HIV-infected patients on HAART was examined The effect of Rp-8-Br-cAMPS on anti-CD3 stimulated proliferation and IL-2 production and the combined effect with exogenous IL-2 were studied in vitro with cells from

13 HIV-infected patients on HAART and 6 uninfected controls. The PKA type I-selective antagonist improved cell proliferation (median 1.5-fold, maximal 2.8-fold) and IL-2 production (median 1.5-fold, maximal 2.4-fold) in T cells from HIV-infected patients on HAART, but not in controls. The addition of IL-2 enhanced proliferation of T cells from HIV-infected patients (approx. 1.9-fold) and that of controls (approx. 1.4-fold), but IL-2 had no effect at the concns. produced by treatment with PKA type I antagonist. However, the combined effect of IL-2 and PKA type I antagonist was additive and resulted in a further increase in T-cell proliferation (median 2.5-fold, maximal 5.8-fold), reaching levels comparable with those of uninfected controls in most of the patients. The authors' findings thus suggest a basis for a novel strategy in treatment of HIV infection by combining IL-2 therapy and treatment modalities counteracting PKA type I activity with HAART.

IT **129735-00-8**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(additive effects of interleukin-2 and protein kinase A type I antagonist on function of T cells from HIV-infected patients on HAART)

RN 129735-00-8 HCAPLUS
CN Adenosine, 8-bromo-, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 27 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:719272 HCAPLUS
DOCUMENT NUMBER: 130:490
TITLE: Use of compounds inhibiting cAMP-dependent protein kinase A as immunomodulating agents for treating immunosuppressive diseases
INVENTOR(S): Tasken, Kjetil; Aandahl, Einar Martin; Aukrust, Pal; Skalhegg, Bjorn S.; Muller, Fredrik; Froland, Stig; Hansson, Vidar
PATENT ASSIGNEE(S): Norway
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9848809		A1	19981105	WO 1998-NO134	19980429
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2288215		AA	19981105	CA 1998-2288215	19980429
AU 9870865		A1	19981124	AU 1998-70865	19980429
AU 738674		B2	20010920		
EP 1024809		A1	20000809	EP 1998-917808	19980429
EP 1024809		B1	20020306		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002501499		T2	20020115	JP 1998-546856	19980429
NZ 501181		A	20020301	NZ 1998-501181	19980429
AT 213944		E	20020315	AT 1998-917808	19980429
PT 1024809		T	20020731	PT 1998-917808	19980429
ES 2171018		T3	20020816	ES 1998-917808	19980429
NO 9905269		A	19991213	NO 1999-5269	19991028
PRIORITY APPLN. INFO.:				NO 1997-1997 A	19970429
				WO 1998-NO134 W	19980429

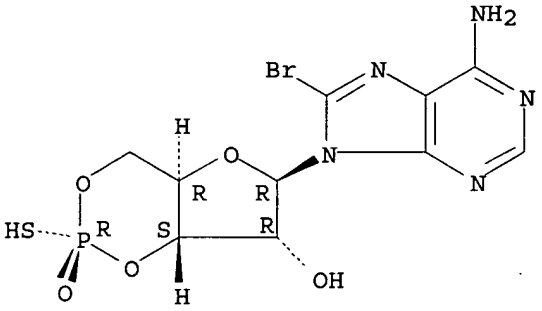
AB Several compds. capable of inhibiting cAMP-dependent protein kinase A (PKA) are used to produce a medicament increasing T-cell proliferation in patients with immunosuppressive diseases. Inhibitors include cAMP analogs, ribozymes, antisense DNA, and peptides binding to the anchoring region of PKA. In T-cells from normal blood donors, TCR/CD3-stimulated T-cell proliferation was inhibited by a cAMP agonist (Sp-8-Br-cAMPS). This effect was almost completely reversed by increasing concns. of complementary antagonist (Rp-8-Br-cAMPS (I)). However, antagonist alone did not alter proliferation of normal T-cells. In contrast, when the TCR/CD3-induced proliferation of T-cells from a HIV-infected patient was investigated, I not only reversed the effect of the complementary agonist, but further increased the proliferation above the levels in untreated cells. When the effect of the antagonist alone was assessed in T-cells from HIV-infected patients, there was a concentration-dependent increase in TCR/CD3-induced proliferation that was more than 2-fold at higher concns. T-cells responding poorly to TCR/CD3 stimulation benefitted most from cAMP antagonist treatment.

IT **129735-00-8 129735-01-9 142754-27-6**
156816-36-3 215597-30-1 215597-33-4
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(as cAMP antagonist; cAMP-dependent protein kinase A inhibitors as immunomodulating agents for treating immunosuppressive diseases)

RN 129735-00-8 HCAPLUS

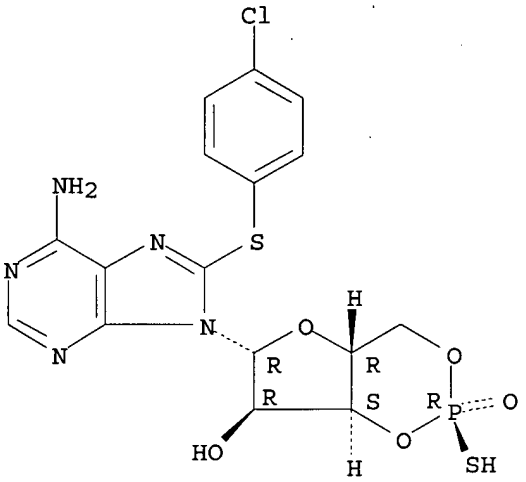
CN Adenosine, 8-bromo-, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



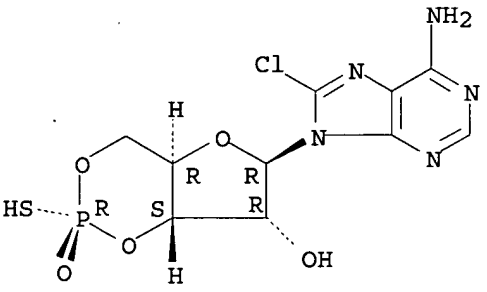
RN 129735-01-9 HCAPLUS
CN Adenosine, 8-[(4-chlorophenyl)thio]-, cyclic 3',5'-[hydrogen (R)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



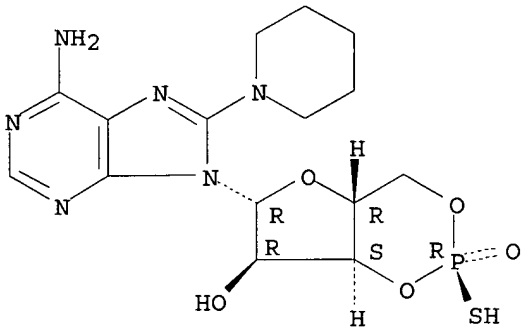
RN 142754-27-6 HCAPLUS
CN Adenosine, 8-chloro-, cyclic 3',5'-[hydrogen (R)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



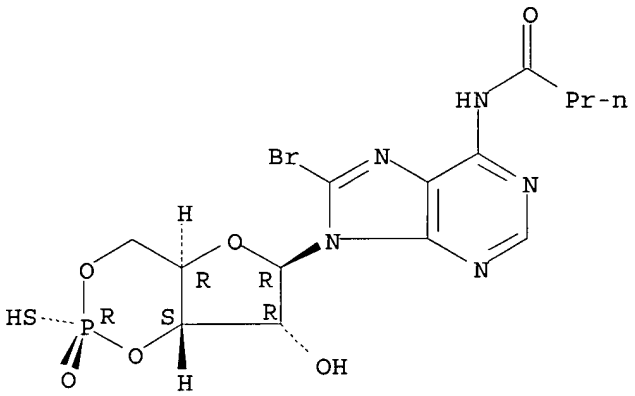
RN 156816-36-3 HCAPLUS
CN Adenosine, 8-(1-piperidinyl)-, cyclic 3',5'-[hydrogen (R)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



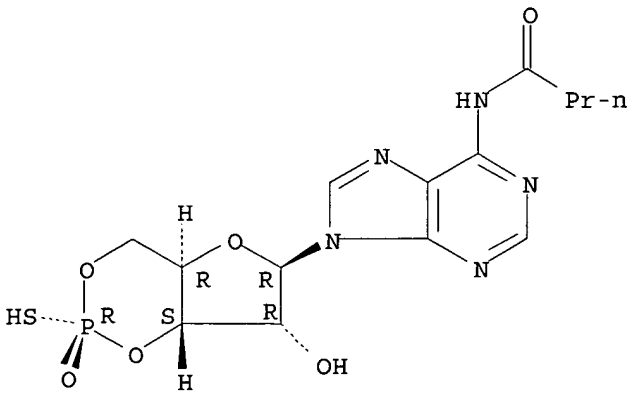
RN 215597-30-1 HCAPLUS
CN Adenosine, 8-bromo-N-(1-oxobutyl)-, cyclic 3',5'-[hydrogen (R)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 215597-33-4 HCAPLUS
CN Adenosine, N-(1-oxobutyl)-, cyclic 3',5'-[hydrogen (R)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 28 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:169417 HCAPLUS
DOCUMENT NUMBER: 128:226257
TITLE: Compositions and methods modulating amyloid precursor protein for treatment of neurological disorders and neurodegenerative diseases, including Alzheimer's disease
INVENTOR(S): Lee, Robert K. K.; Wurtman, Richard J.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809523	A1	19980312	WO 1997-US15321	19970905
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2279651	AA	19980312	CA 1997-2279651	19970905
EP 1006798	A1	20000614	EP 1997-941386	19970905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

US 1996-25507P	P	19960905
US 1997-33765P	P	19970115
WO 1997-US15321	W	19970905

AB It has been discovered that the stimulation of β-adrenergic receptors, which activate cAMP formation, give rise to increased APP and GFAP synthesis in astrocytes. Hence, the in vitro or in vivo exposure of neuronal cells to certain compns. comprising β-adrenergic receptor ligands or agonists, including, e.g., norepinephrine, isoproterenol and the like, increases APP mRNA transcription and consequent APP overprodn. These increases are blocked by β-adrenergic receptor antagonists, such as propranolol. The in vitro or in vivo treatment of these cells with 8Br-cAMP, prostaglandin E2 (PG E2), forskolin, and nicotine ditartrate also increased APP synthesis, including an increase in mRNA and holoprotein levels, as well as an increase in the expression of glial fibrillary acidic protein (GFAP). Compns. and methods are disclosed of regulating APP overexpression and mediating reactive astrogliosis through cAMP signaling or the activation of β-adrenergic receptors. It has further been found that the increase in APP synthesis caused by 8Br-cAMP, PG E2, forskolin, or nicotine ditartrate is inhibited by immunosuppressants or anti-inflammatory agents, such as cyclosporin A, and FK-506 (tacrolimus), as well as ion-channel modulators, including ion chelating agents such as EGTA, or calcium/calmodulin kinase inhibitors, such as KN93. The present invention has broad implications in the alleviation, treatment, or prevention of neurol. disorders and neurodegenerative diseases, including Alzheimer's disease.

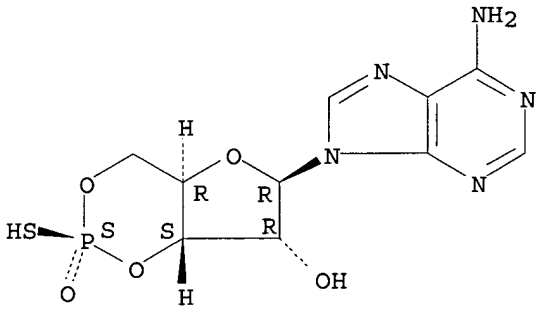
IT **93602-66-5**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(amyloid precursor protein modulation in treatment of neurol. and neurodegenerative diseases, including Alzheimer's disease)

RN 93602-66-5 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen (S)-phosphorothioate], compd. with N,N-diethylethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

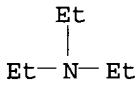
CRN 71774-13-5
CMF C10 H12 N5 O5 P S

Absolute stereochemistry.



CM 2

CRN 121-44-8
CMF C6 H15 N



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 29 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:434799 HCAPLUS
DOCUMENT NUMBER: 129:170140
TITLE: Protein kinase A type I antagonist restores immune responses of T cells from HIV-infected patients
AUTHOR(S): Aandahl, Einar Martin; Aukrust, Pal; Skalhegg, Bjorn S.; Muller, Fredrik; Froland, Stig S.; Hansson, Vidar; Tasken, Kjetil
CORPORATE SOURCE: Institute of Medical Biochemistry, University of Oslo, Oslo, N-0317, Norway
SOURCE: FASEB Journal (1998), 12(10), 855-862
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CAMP-dependent protein kinase A (PKA) type I has been established as an acute inhibitor of T cell activation. For this reason, we investigated the possible role of PKA type I in HIV-induced T cell dysfunction. T cells from HIV-infected patients have increased levels of cAMP and are more sensitive to inhibition by cAMP analog than are normal T cells. A

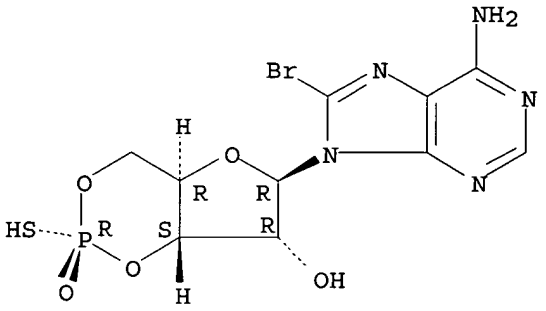
PKA type I-selective antagonist increases the impaired proliferation of T cells from HIV-infected patients to normal or subnormal levels (up to 2.8-fold). Follow-up of patients after initiation of highly active antiretroviral treatment revealed that a majority of patients have a persistent T cell dysfunction that is normalized by incubation of T cells with Rp-8-Br-cAMPS. These observations imply that increased activation of PKA type I may contribute to the progressive T cell dysfunction in HIV infection and that PKA type I may be a potential target for immunomodulating therapy.

IT **129735-00-8**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(protein kinase A type I antagonist restores immune responses of T cells from HIV-infected patients)

RN 129735-00-8 HCAPLUS

CN Adenosine, 8-bromo-, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 30 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:572406 HCAPLUS

DOCUMENT NUMBER: 129:285575

TITLE: Quantitative structure-activity relations for the relative affinities of cAMP derivatives with large substituents in positions 2 and 8 for the four different regulatory sites of a protein kinase

AUTHOR(S): Liauw, Susanne; Iwitzki, Franz; Muresan, Sorel; Bologa, Cristian; Chiriac, Adrian; Kurunczi, Ludovic; Simon, Zeno; Jastorff, Bernd

CORPORATE SOURCE: Dep. Bioorganic Chem., Univ. Bremen, Bremen, D-2000, Germany

SOURCE: Revue Roumaine de Chimie (1998), 43(3), 241-253
CODEN: RRCHAX; ISSN: 0035-3930

PUBLISHER: Editura Academiei Romane

DOCUMENT TYPE: Journal

LANGUAGE: English

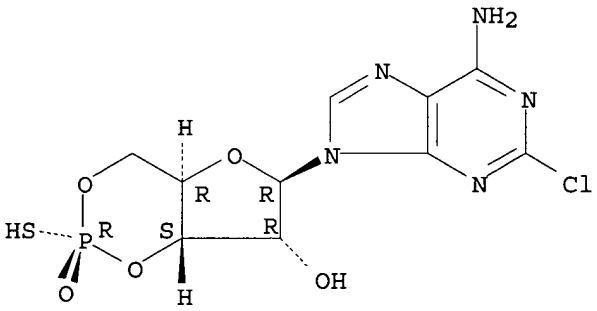
AB QSAR's by the MTD-method for a series of 32 derivs. of cAMP with large substituents in position 8 and for a series of 21 derivs. with large substituents in position 2 are obtained. Thiophosphoric acid derivs. are also included. As structural parameters, the relative nitrogen base lipophilicity, the presence of an equatorial or axial S atom and the presence of aliphatic amino group, protonated at pH = 7 are considered. Satisfactory correlational results, including a cross-validation like procedure, are obtained in most cases. The results emphasize structural

features important for binding to four sites (AI, BI, AII, and BII) of two different protein phosphokinases (cAKI and cAKII). The synthesis and characterization of eight new compds. are also described.

IT **124844-92-4 124854-63-3 142754-27-6**
142754-28-7 156816-35-2 156816-36-3,
Adenosine, 8-(1-piperidinyl)-, cyclic 3',5'-(hydrogen phosphorothioate), (R)- **214272-09-0 214272-10-3 214276-87-6**
214276-94-5
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(quant. structure-activity relations for the relative affinities of cAMP derivs. for protein kinase regulatory sites)

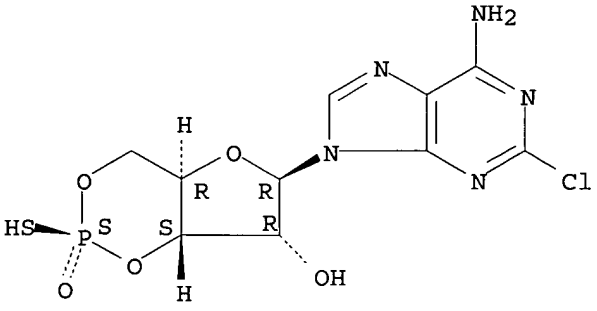
RN 124844-92-4 HCAPLUS
CN Adenosine, 2-chloro-, cyclic 3',5'-[(R)-hydrogen phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



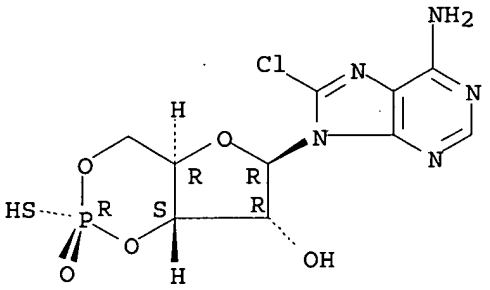
RN 124854-63-3 HCAPLUS
CN Adenosine, 2-chloro-, cyclic 3',5'-[(S)-hydrogen phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



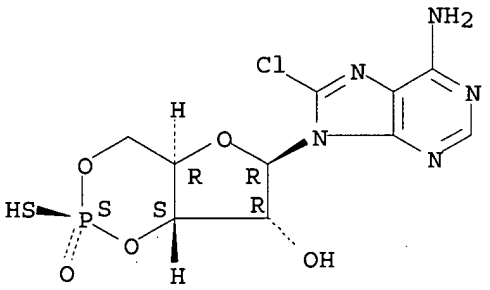
RN 142754-27-6 HCAPLUS
CN Adenosine, 8-chloro-, cyclic 3',5'-[hydrogen (R)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



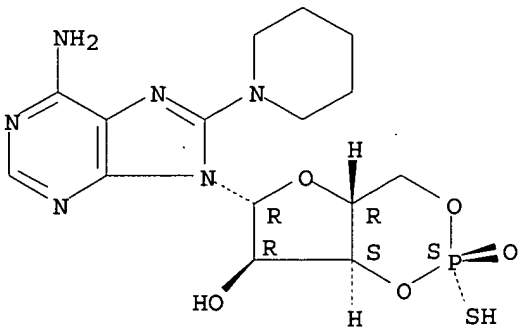
RN 142754-28-7 HCAPLUS
CN Adenosine, 8-chloro-, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



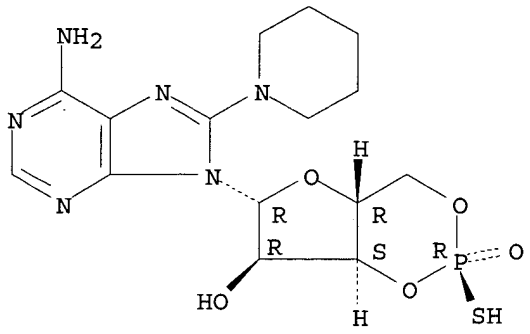
RN 156816-35-2 HCAPLUS
CN Adenosine, 8-(1-piperidinyl)-, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



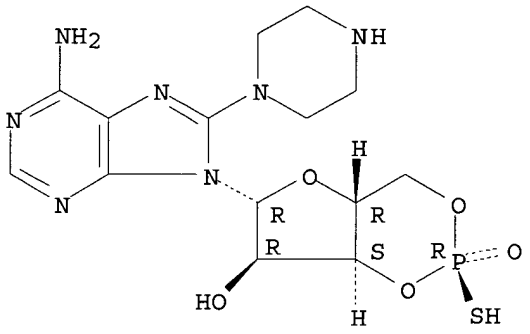
RN 156816-36-3 HCAPLUS
CN Adenosine, 8-(1-piperidinyl)-, cyclic 3',5'-[hydrogen (R)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



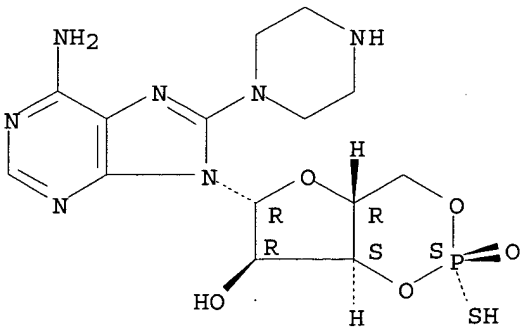
RN 214272-09-0 HCAPLUS
CN Adenosine, 8-(1-piperazinyl)-, cyclic 3',5'-[(R)-hydrogen phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



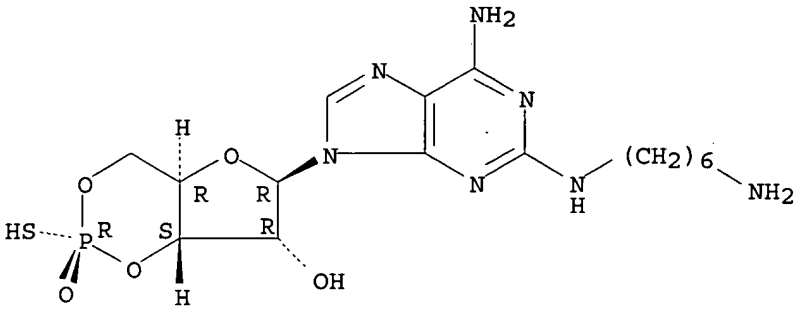
RN 214272-10-3 HCAPLUS
CN Adenosine, 8-(1-piperazinyl)-, cyclic 3',5'-[(S)-hydrogen phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



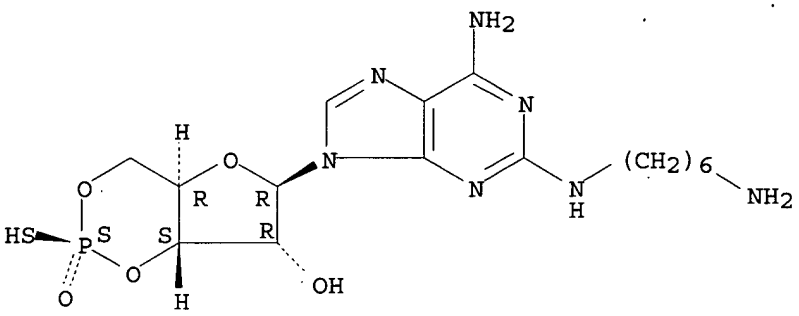
RN 214276-87-6 HCAPLUS
CN Adenosine, 2-[(6-aminohexyl)amino]-, cyclic 3',5'-[(R)-hydrogen phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 214276-94-5 HCAPLUS
CN Adenosine, 2-[(6-aminohexyl)amino]-, cyclic 3',5'-[(S)-hydrogen phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



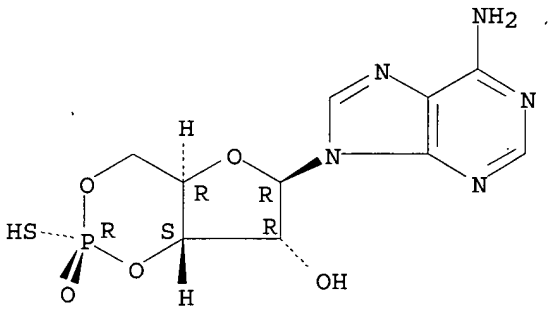
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 31 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:285160 HCAPLUS
DOCUMENT NUMBER: 129:62911
TITLE: Protein kinase A inhibitors reverse histamine-mediated regulation of IL-5 secretion
AUTHOR(S): Poluektova, Larisa Y.; Khan, Manzoor M.
CORPORATE SOURCE: Department of Pharmaceutical and Adm. Sciences, Creighton University, Omaha, NE, 68178, USA
SOURCE: Immunopharmacology (1998), 39(1), 9-19
CODEN: IMMUDP; ISSN: 0162-3109
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Histamine and IL-5 are important autacoid mediators involved in the etiol. of allergic diseases. IL-5 is the main factor of eosinophilic reactions in allergy. It has been suggested that the protein kinase A-dependent (PKA) pathway of signal transduction may play the main role in histamine-induced elevation of IL-5 production This study was designed to investigate the effects of the inhibitors of regulatory and catalytic subunits of PKA on histamine-mediated elevation of IL-5 production In this study, histamine at a concentration of 10-4-10-6 M enhanced IL-5 production in D10.G4.1 cells, a mouse Th2 helper cell line. Pretreatment of this cell line with histamine at a concentration of 10-4 M for 6-9 h had the maximum stimulatory effects (226-420%) on IL-5 production Other cAMP-elevating agents

including forskolin and Bt2-cAMP produced similar effects. The PKA inhibitors N-[2-(methylamino)ethyl]-5-isoquinolinesulfonamide (H-8) and the Rp-diastereomer of adenosine cyclic 3',5'-phosphorothioate (Rp-cAMPS) were used for the inhibition of catalytic and regulatory subunits of PKA, resp. Pretreatment of D10.G4.1 cells with H-8 at a concentration of 10-5 M completely prevented the effects of histamine at a concentration range of 10-6-10-4 M. Rp-cAMPS at 10-5 M also prevented histamine-induced stimulation. Neither inhibitor affected IL-5 production when tested alone. These observations suggest a role for PKA in histamine-mediated increase in IL-5 production

IT **73208-40-9**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of histamine-mediated increase in interleukin-5 production by protein kinase A inhibitors)
RN 73208-40-9 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 32 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:165500 HCAPLUS
DOCUMENT NUMBER: 126:166497
TITLE: Method and composition for treating cystic fibrosis
INVENTOR(S): Drumm, Mitchell L.; Kelley, Thomas J.
PATENT ASSIGNEE(S): Case Western Reserve University, USA
SOURCE: U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 299,013, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5602110	A	19970211	US 1995-378638	19950126
WO 9606612	A1	19960307	WO 1995-US11008	19950829
W: AU, CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9535415	A1	19960322	AU 1995-35415	19950829
PRIORITY APPLN. INFO.:			US 1994-299013 B2	19940831
			US 1995-378638 A	19950126

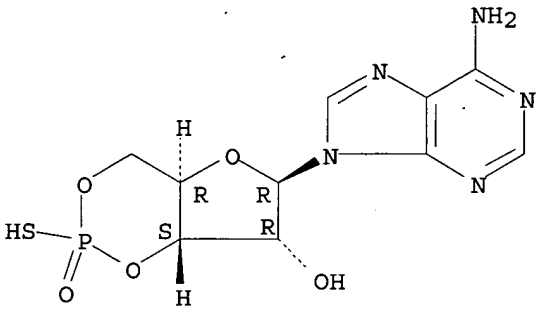
WO 1995-US11008 W 19950829

AB Cystic fibrosis is treated by administering to a patient a first component, a second component, and preferably a third component. The first component is an inhibitor which is specific for a cGMP-inhibited type III cAMP phosphodiesterase, preferably milrinone or amrinone; the second component is an adenylate cyclase activator, preferably forskolin, isoproterenol or albuterol; the third component is cAMP or a cAMP analog which activates protein kinase A. The components are administered by aerosolization or nebulization. Cystic fibrosis transmembrane conductance regulator-mediated chloride permeability is activated in cystic fibrosis cells by the synergistic action of an adenylate cyclase activator and a type III phosphodiesterase inhibitor.

IT **23645-17-2**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(aerosols containing cAMP phosphodiesterase inhibitor and adenylate cyclase activator and protein kinase A activator for treatment of cystic fibrosis)

RN 23645-17-2 HCAPLUS
CN Adenosine, cyclic 3',5'-(hydrogen phosphorothioate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



5197 X

L19 ANSWER 33 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:521383 HCAPLUS
DOCUMENT NUMBER: 127:215009
TITLE: Effect of Rp diastereoisomer of adenosine 3',5' cyclic-monophosphothioate on the cAMP-dependent relaxation of smooth muscle
AUTHOR(S): Perez-Vallina, Jose R.; Revuelta, M.Pilar; Cantabrana, Begona; Hidalgo, Agustin
CORPORATE SOURCE: Laboratorio de Farmacologia, Dpto. Medicina, Facultad de Medicina, Oviedo, 33006, Spain
SOURCE: Life Sciences (1997), 61(9), 869-880
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

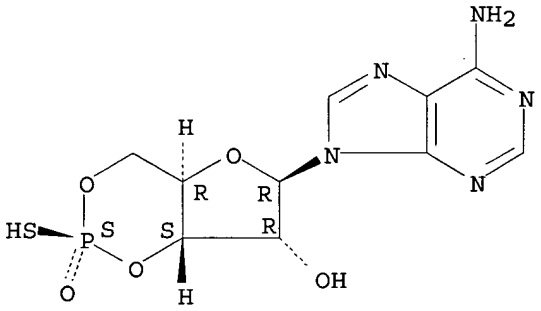
AB The effect of Rp diastereoisomer of adenosine 3',5'-cyclic monophosphothioate (Rp-cAMPS) on relaxation elicited by histamine (1-100 μM), forskolin (1-60 μM), papaverine (1-100 μM), vinpocetine (1-100 μM), rolipram (0.1-1 mM), Sp-cAMPS (10-300 μM), 8-BrcAMP (10 μM-1 mM) and 8-BrcGMP (3 μM-1 mM) of the previous vanadate-induced contraction was assayed. The effect of Rp-cAMPS on the relaxing effect

produced by forskolin, papaverine, vinpocetine, rolipram, Sp-cAMPS and 8-BrcAMP in KCl-induced tonic contraction was also assayed. Histamine, forskolin, papaverine, rolipram, Sp-cAMPS, 8-BrcAMP and 8-BrcGMP, but not vinpocetine, relaxed the vanadate-induced contractions in rat uterus incubated in medium lacking calcium plus EDTA in a concentration-dependent way. Rp-cAMPS (1-300 μM) had no effect on vanadate contraction. However, it antagonized the relaxation elicited by histamine and papaverine, but not that of forskolin, rolipram, Sp-cAMPS, 8-BrcAMP and 8-BrcGMP. Forskolin, papaverine, vinpocetine, rolipram and 8-BrcAMP, but not Sp-cAMPS, relaxed the KCl-induced contraction. Rp-cAMPS antagonized the relaxation elicited by forskolin, papaverine and vinpocetine, but not that of rolipram and 8-BrcAMP. The results suggest that: (a) Rp-cAMPS is an effective cAMP-dependent protein kinase (PKA) inhibitor that could be used to study the involvement of cAMP on drug-induced response in smooth muscle, and (b) the effects of Sp-cAMPS, 8-BrcAMP and rolipram were independent of the activation of protein kinases.

IT **71774-13-5 73208-40-9**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(effect of Rp diastereoisomer of adenosine 3',5' cyclic-monophosphothioate on cAMP-dependent relaxation of smooth muscle by relaxing agents)

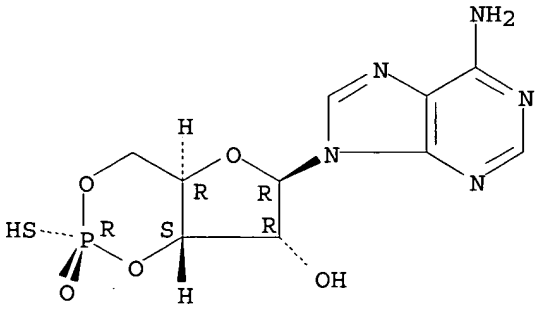
RN 71774-13-5 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 73208-40-9 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

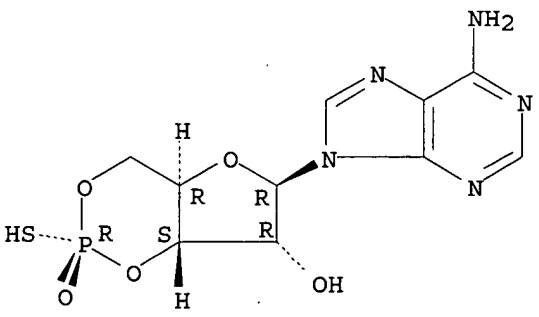


L19 ANSWER 34 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:90387 HCAPLUS
DOCUMENT NUMBER: 128:225926
TITLE: Effects of pimobendan and its active metabolite, UD-CG 212Cl, on Ca2+-activated K+ channels in vascular smooth-muscle cells
AUTHOR(S): Chen, Cheun-He; Nakaya, Yutaka; Minami, Kazushi; Kubo, Masahiro
CORPORATE SOURCE: Department Nutrition, School Medicine, University Tokushima, Tokushima, Japan
SOURCE: Journal of Cardiovascular Pharmacology (1997), 30(6), 739-743
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Expts. were done to clarify the mechanisms of activation of Ca2+-dependent K+ (KCa) channels by pimobendan, a cardiotonic and vasodilator agent with phosphodiesterase-inhibiting properties, and its main metabolite, UD-CG 212Cl, in vascular smooth-muscle cells from porcine coronary arteries. Both pimobendan and UD-CG 212Cl induced relaxation of porcine coronary artery strips. However, in the presence of 100 μM Rp-cAMPS (Rp diastereomer of adenosine cyclic 3',5'-phosphorothioate), a membrane-permeable antagonist of cAMP, the effects of pimobendan decreased. Addition of 1 μM pimobendan activated KCa channels in cell-attached patches, and this increase was suppressed by 100 nM H-89, a cAMP-dependent protein-kinase inhibitor. Pimobendan was ineffective in altering the activity of KCa channels in inside-out patches. In contrast, UD-CG 212Cl, at 1 μM, activated KCa channels not only in cell-attached patches but also in inside-out patches. The presence of 100 nM H-89 also inhibited UD-CG 212Cl-induced KCa channel activity but to a lesser degree than that induced by pimobendan in cell-attached patches. There are apparently 2 mechanisms of activation of KCa channels by pimobendan and UD-CG 212Cl. Activation by pimobendan occurs primarily through the cAMP pathway, whereas UD-CG 212 Cl activates KCa channels directly as well as through the cAMP pathway.

IT **73208-40-9**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(effects of pimobendan and its metabolite UD-CG 212Cl on calcium-activated potassium channels in coronary artery inhibition by)
RN 73208-40-9 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

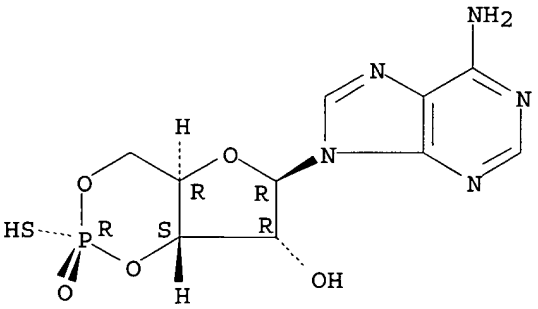
L19 ANSWER 35 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:419349 HCAPLUS
DOCUMENT NUMBER: 127:75941
TITLE: Protein kinase A inhibitor attenuates levodopa-induced motor response alterations in the hemi-parkinsonian rat
AUTHOR(S): Oh, Justin D.; Del Dotto, Paolo; Chase, Thomas N.
CORPORATE SOURCE: Experimental Therapeutics Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Neuroscience Letters (1997), 228(1), 5-8
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chronic administration of levodopa, the standard treatment for Parkinson's disease, is ultimately associated with disabling alterations in motor response. To evaluate the possible contribution of striatal cAMP-dependent protein kinase A (PKA) signaling pathways to these response modifications, the acute effects of a PKA inhibitor, Rp-cAMPS (Rp-diastereoisomer of adenosine cyclic 3',5'-phosphorothioate), on motor response changes attending chronic, twice-daily administration of levodopa were measured in 6-hydroxydopamine-lesioned hemi-parkinsonian rats. A single intrastriatal injection of Rp-cAMPS (2.5 or 25 μg) dose-dependently attenuated both the shortened duration and augmented intensity of levodopa-induced turning. Rp-cAMPS completely normalized motor responses to a dopamine D1 agonist (SKF 38392), but had no effect on those to a dopamine D2 agonist (quinpirole). These results suggest that D1 receptor-mediated PKA activation may contribute to the development of the altered motor responses associated with chronic levodopa treatment.

IT **73208-40-9**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(parkinson-like motor response alterations induced by chronic levodopa attenuation by)

RN 73208-40-9 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 36 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:603959 HCAPLUS
DOCUMENT NUMBER: 123:17877
TITLE: Method of inducing vasorelaxation to treat pulmonary hypertension
INVENTOR(S): Lawson, Charles A.; Pinsky, David J.; Smerling, Arthur; Stern, David M.
PATENT ASSIGNEE(S): Trustees of Columbia University in the City of New York, USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

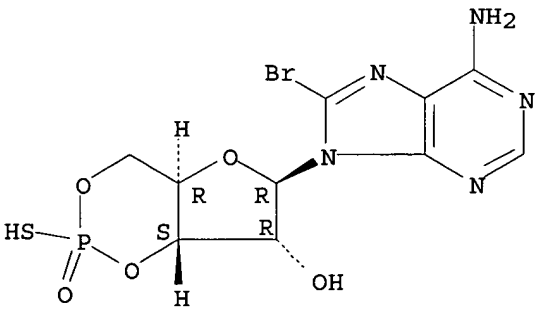
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9509636	A1	19950413	WO 1994-US11248	19941004
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5728705	A	19980317	US 1993-131984	19931004
AU 9479652	A1	19950501	AU 1994-79652	19941004
US 5968911	A	19991019	US 1997-362571	19970218
PRIORITY APPLN. INFO.:			US 1993-131984 A	19931004
			WO 1994-US11248 W	19941004

AB A method of selectively decreasing pulmonary vascular resistance in a subject comprises administering endobronchially a drug chosen from cAMP analogs, cGMP analogs, phosphodiesterase inhibitors, nitric oxide precursors, nitric oxide donors, and nitric oxide analogs, as aerosol solns. or powders.

IT **152322-58-2**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(aerosols containing vasorelaxants for treatment of pulmonary hypertension)

RN 152322-58-2 HCAPLUS
CN Adenosine, 8-bromo-, cyclic 3',5'-(hydrogen phosphorothioate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 37 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:113512 HCAPLUS
DOCUMENT NUMBER: 124:156073
TITLE: cAMP derivatives as synovial membrane cell

proliferation inhibitors and pharmaceutical compositions containing cAMP derivatives for treatment of chronic arthrorheumatism

INVENTOR(S): Higaki, Megumi; Sakane, Takeshi; Mizushima, Yutaka; Yasumoto, Takashi; Morisawa, Yoshitomi

PATENT ASSIGNEE(S): Ltt Inst Co Ltd, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07324035	A2	19951212	JP 1994-116194	19940530
PRIORITY APPLN. INFO.:			JP 1994-116194	19940530

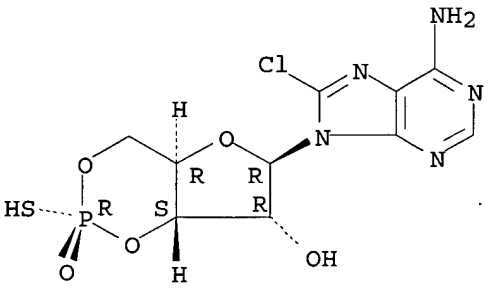
AB CAMP derivs. as synovial membrane cell proliferation inhibitors and pharmaceutical compns. containing CAMP derivs. for treatment of chronic arthrorheumatism are claimed. The compds. markedly inhibited the proliferation of synovial membrane cells in cultures. Capsules were formulated containing 8-chloro-cAMP 5μg, lactose 148, corn starch 50, and magnesium stearate 1.5g.

IT **142754-27-6 142754-28-7**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cAMP derivs. as synovial membrane cell proliferation inhibitors and pharmaceutical compns. containing CAMP derivs. for treatment of chronic arthrorheumatism)

RN 142754-27-6 HCAPLUS

CN Adenosine, 8-chloro-, cyclic 3',5'-[hydrogen (R)-phosphorothioate] (9CI) (CA INDEX NAME)

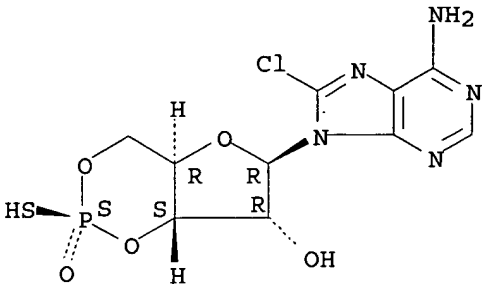
Absolute stereochemistry.



RN 142754-28-7 HCAPLUS

CN Adenosine, 8-chloro-, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 38 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:559572 HCAPLUS
DOCUMENT NUMBER: 123:790
TITLE: Evaluation of cAMP involvement in cannabinoid-induced antinociception
AUTHOR(S): Cook, Stacie A.; Welch, Sandra P.; Lichtman, Aron H.; Martin, Billy R.
CORPORATE SOURCE: Dep. Pharmacology Toxicology, Medical College Virginia, Virginia Commonwealth University, Richmond, VA, 23298-0613, USA
SOURCE: Life Sciences (1995), 56(23/24), 2049-56
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

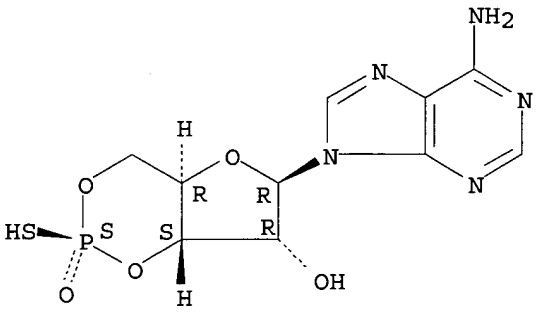
AB It has been proposed that cannabinoids act at a Gi protein-coupled receptor to produce antinociception. One action of Gi-proteins is to decrease intracellular cAMP via inhibition of adenylyl cyclase activity. Although cannabinoid inhibition of forskolin-stimulated adenylyl cyclase is used as a confirmation of functional cannabinoid receptors, it is unknown whether this 2nd messenger system specifically mediates cannabinoid-induced antinociception. This in vivo study was conducted with 2 enantiomeric cAMP analogs: Rp-cAMPS [Rp-adenosine 3',5'-cyclic phosphorothioate (an antagonist)] and Sp-cAMPS [Sp-adenosine 3',5'-cyclic phosphorothioate (an agonist)], and with the cAMP agonist Cl-cAMP [8-(4-chlorophenylthio)adenosine 3',5'-monophosphate cyclic Na salt], to test the hypothesis that cannabinoid-induced antinociception is due to decreased adenylyl cyclase activity. None of the above cAMP analogs, forskolin, or 1,9-dideoxyforskolin affected Δ9-tetrahydrocannabinol- or CP-55,940-induced antinociception produced by intrathecal or intracerebroventricular (i.c.v.) injections into mice. Expts. were also conducted to investigate whether i.c.v. administration of Sp-cAMPS would block i.c.v. cannabinoid-induced antinociception in rats. Sp-cAMPS failed to block CP-55,940-induced antinociception. However, Sp-cAMPS produced hyperexcitability and reactive behavior, indicating that it did elicit a pharmacol. effect. Although adenylyl cyclase may mediate other cannabinoid-induced actions, these results do not support the hypothesis that it is involved in cannabinoid-induced antinociception. Other effector systems, such as Ca2+ or K+ channels coupled to cannabinoid receptors, may mediate cannabinoid-induced antinociception.

IT **71774-13-5 73208-40-9**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(role of cAMP and adenylyl cyclase in relation to cannabinoid-induced antinociception response to)

RN 71774-13-5 HCAPLUS

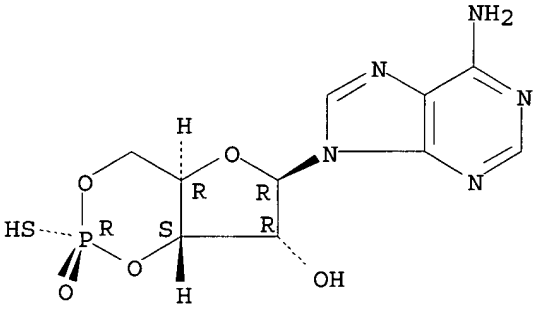
CN Adenosine, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 73208-40-9 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 39 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:807476 HCAPLUS
DOCUMENT NUMBER: 123:217972
TITLE: The specific type IV phosphodiesterase inhibitor rolipram differentially regulates the proinflammatory mediators TNF-α and nitric oxide
AUTHOR(S): Greten, Tim F.; Eigler, Andreas; Sinha, Bhanu; Moeller, Jochen; Endres, Stefan
CORPORATE SOURCE: Medizinische Klinik, Ludwig-Maximilians-Univ., Munich, D-80336, Germany
SOURCE: International Journal of Immunopharmacology (1995), 17(7), 605-10
CODEN: IJIMDS; ISSN: 0192-0561
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of the specific type IV phosphodiesterase inhibitor rolipram on intracellular cAMP concentration and on NO and tumor necrosis factor-α (TNF) formation was studied in the murine macrophage cell line RAW 264.7. Rolipram concentration-dependently increased NO accumulation in lipopolysaccharide-stimulated macrophages, whereas TNF synthesis was suppressed to <30% of control values. This was accompanied by an increase

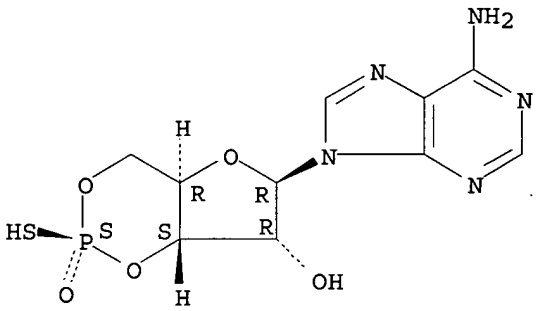
of cAMP concentration The stable cAMP analog (S)-p-adenosine 3',5'-cyclic phosphorothioate also concentration-dependently enhanced NO formation by these cells. Apparently, it is the elevation of cAMP in RAW 264.7 cells by rolipram that decreases TNF synthesis and increases NO formation.

IT **71774-13-5**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(nitric oxide production by macrophage stimulation by)

RN 71774-13-5 HCAPLUS

CN Adenosine, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 40 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:656486 HCAPLUS

DOCUMENT NUMBER: 123:131990

TITLE: Evidence for several pathways of biological response to hydrolyzable cAMP-analogs using a model system of apoptosis in IPC-81 leukemia cells

AUTHOR(S): Ruchaud, S.; Zorn, M.; Davilar-Villar, E.; Genieser, H. G.; Hoffmann, C.; Gjersten, B. T.; Doeskeland, S. O.; Jastorff, B.; Lanoote, M.

CORPORATE SOURCE: Centre G. Hayfem, Hopital St-Louis, Paris, Fr.

SOURCE: Cellular Pharmacology (1995), 2(3), 127-40
CODEN: CEPHEG; ISSN: 1351-3214

PUBLISHER: Macmillan Scientific & Medical Division

DOCUMENT TYPE: Journal

LANGUAGE: English

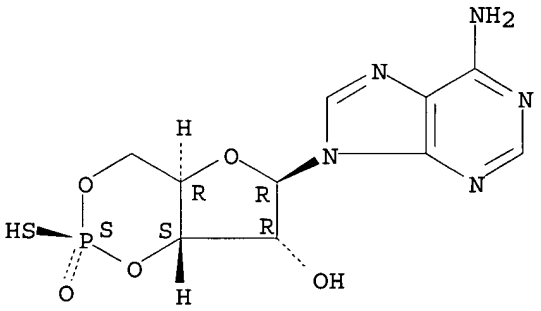
AB Degradable and undegradable cAMP analogs with a wide range of rationally selected (testkit concept) chemical modifications were studied for their apoptotic potency in the rat IPC-81 model for acute myelocytic leukemia. The biol. activity of corresponding 5'AMP and adenosine metabolites was compared. To discriminate a cA-kinase response from non-kinase effects the authors used a subclone of the IPC-81 line with a sub-responsiveness to cA-kinase I activation by cAMP analogs. As proven by HPLC, only cAMP analogs with an axial (Sp) and equatorial (Rp) substitution at the phosphate moiety were partially or totally resistant against metabolism in cell culture. Heat inactivation of serum only reduced but not prevented the formation of metabolites. The results gave different dose responses due to the type of modification at the signal mols. and the type of cell line. Undegradable cAMP analogs only induced apoptosis via the cA-kinase pathway in the two cell lines; most efficiently through the highly lipophilic, resistant and cA-kinase specific analog Sp-DCl-cBIMPS. The lipophilic cAMP antagonist Rp-8Cl-cAMPS inhibited the induction of apoptosis by its corresponding Sp-8Cl-cAMPS in a dose-dependent manner.

Degradable cAMP analogs act via the cyclic nucleotides and/or their metabolites. Rationale for the different types of responses based on structure activity relations are discussed and mechanisms of actions are proposed. The authors' study supports an essential participation of the cAMP signaling pathway in induction of apoptosis, if a highly cooperative way of cell death is induced. Exclusively via the cAMP signaling cascade, an analog will act only if the derivative is undegradable, highly membrane permeable and a potent cA-kinase activator. Degradable analogs exhibit their effects through diverse mechanisms. Detailed biochem. and cell biol. studies with the complete set of catabolites and metabolites of those derivs., which exhibit the highest activity, allow the design of a new generation of nucleosides and nucleotides with high, hopefully cell type selective, potential for apoptosis in tumor cells.

IT **71774-13-5 73208-40-9 124854-63-3**, Adenosine, 2-chloro-, cyclic 3',5'-(hydrogen phosphorothioate), (S)- **127634-20-2 142754-27-6 142754-28-7**
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(evidence for several pathways of biol. response to hydrolyzable cAMP-analogs using a model system of apoptosis in IPC-81 leukemia cells)

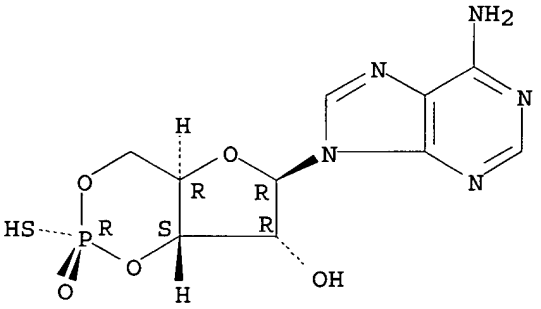
RN 71774-13-5 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



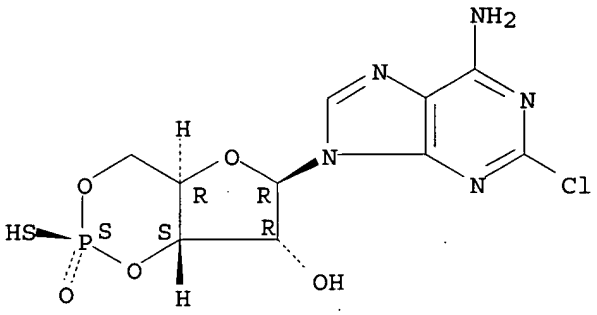
RN 73208-40-9 HCAPLUS
CN Adenosine, cyclic 3',5'-[hydrogen [P(R)]-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



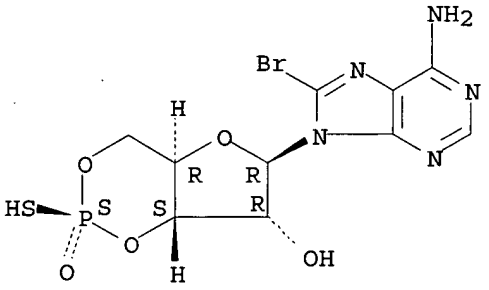
RN 124854-63-3 HCAPLUS
CN Adenosine, 2-chloro-, cyclic 3',5'-[(S)-hydrogen phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



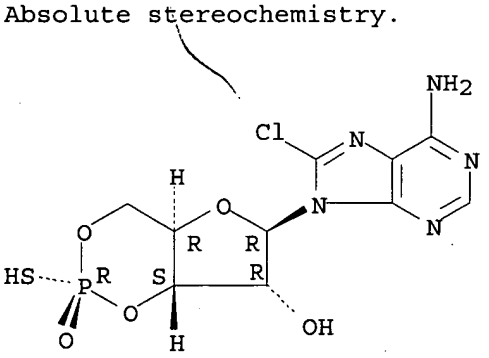
RN 127634-20-2 HCAPLUS
CN Adenosine, 8-bromo-, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



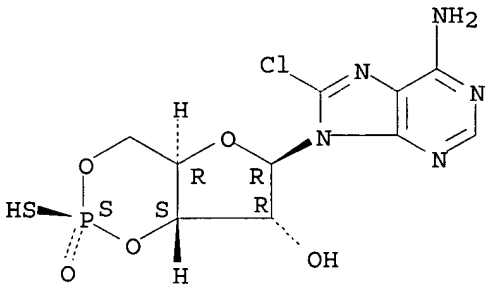
RN 142754-27-6 HCAPLUS
CN Adenosine, 8-chloro-, cyclic 3',5'-[hydrogen (R)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 142754-28-7 HCAPLUS
CN Adenosine, 8-chloro-, cyclic 3',5'-[hydrogen (S)-phosphorothioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 41 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1993-368399 [46] WPIDS
DOC. NO. CPI: C1993-163448
TITLE: Inhibiting proliferation of cells with phosphoro-thioate derivative of **cAMP** - modified at C6 or C8 position, for **treating** cancer and leukaemia, resistant to hydrolysis to toxic metabolites.
DERWENT CLASS: B02
INVENTOR(S): CHO-CHUNG, Y S; GENIESER, H; JASTORFF, B
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES; (USSH) US DEPT HEALTH & HUMAN SERVICE
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9321929	A1	19931111	(199346)*	EN	80
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP KR					
AU 9342266	A	19931129	(199411)		
US 5843916	A	19981201	(199904)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9321929	A1		WO 1993-US4093	19930430
AU 9342266	A		AU 1993-42266	19930430
US 5843916	A	Cont of	US 1992-877523	19920501
			US 1994-225097	19940408

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9342266	A	Based on	WO 9321929

PRIORITY APPLN. INFO: US 1992-877523 19920501; US 1994-225097 19940408

AB WO 9321929 A UPAB: 19940103
Proliferation of cells is inhibited by contacting them with a **phosphorothioate** derivative (I) of a **cAMP** modified at C6 and/or C8 positions of adenine, or its pharmaceutically acceptable salt.
Partic. (I) is a modified 8-(chloro, bromo or iodo)-**cAMP**, specifically the Rp-diastereomer (equatorial exocyclic sulphur), (Ia), of

8-chloro-**cAMPS** or the 5p(axial)-diastereomer of 8-bromo-**cAMPS** (Ib). Opt. the cells are also **treated** with a second **cAMP** derivative (II).

USE/ADVANTAGE - The **treatment** is especially applied to cancerous or leukaemic cells and (I) antagonise **cAMP**-dependent protein kinases. Especially the cells being **treated** contain more of the RI alpha isoform of the **cAMP** receptor than the RII beta isoform. (I) are more resistant to hydrolysis to toxic metabolites than **cAMP** derivs. not containing S in the phosphate gp. **Treatment** with (I), and opt. (II), also increases cell differentiation and may be effective against cancer cells resistant to known **cAMP** analogues or agents which increase intracellular **cAMP** levels. The dose of (I) is enough to provide a serum concentration of 0.1-100 micron, and is pref. admin. in conventional oral formulations.

Dwg.0/11

L19 ANSWER 42 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1992-201452 [25] WPIDS
CROSS REFERENCE: 1997-365927 [34]; 2000-099854 [09]
DOC. NO. CPI: C1992-091607
TITLE: New antisense oligo-nucleotide(s) for **treating** cancers - inhibit expression of the RI-alpha subunit of type I **cAMP** dependent protein kinase.
DERWENT CLASS: B04 D16
INVENTOR(S): YOON, S C; YOON, S
PATENT ASSIGNEE(S): (FORY-N) FORYOU CORP; (YOON-I) YOON S C; (YOON-I) YOON S
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 490077	A1	19920617	(199225)*	EN	26
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
CA 2054325	A	19920503	(199230)	FR	
US 5271941	A	19931221	(199351)		20
JP 06211889	A	19940802	(199435)		22
JP 08310958	A	19961126	(199706)		18
US 5627158	A	19970506	(199724)		21
EP 490077	B1	19970806	(199736)	EN	21
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
DE 69127175	E	19970911	(199742)		
ES 2104644	T3	19971016	(199748)		
US 5691317	A	19971125	(199802)		12
JP 2719060	B2	19980225	(199813)		25
KR 171210	B1	19990201	(200039)		
JP 3150609	B2	20010326	(200126)		22
CA 2488792	A1	19920503	(200515)	EN	
CA 2054325	C	20050315	(200522)	EN	

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 490077	A1		EP 1991-118628	19911031
CA 2054325	A		CA 1991-2054325	19911028
US 5271941	A	CIP of	US 1990-607113	19901102
		CIP of	US 1991-680198	19910405
			US 1991-702163	19910520
JP 06211889	A		JP 1991-278407	19910930
JP 08310958	A	Div ex	JP 1991-278407	19910930

			JP 1996-72826	19910930
US 5627158	A	CIP of	US 1990-607113	19901102
		CIP of	US 1991-680198	19910405
		Div ex	US 1991-702163	19910520
			US 1993-60984	19930514
EP 490077	B1		EP 1991-118628	19911031
		Related to	EP 1997-100277	19911031
DE 69127175	E		DE 1991-627175	19911031
			EP 1991-118628	19911031
ES 2104644	T3		EP 1991-118628	19911031
US 5691317	A	CIP of	US 1990-607113	19901102
		CIP of	US 1991-680198	19910405
		Div ex	US 1991-702163	19910520
		Cont of	US 1993-60984	19930514
			US 1995-383742	19950202
JP 2719060	B2		JP 1991-278407	19910930
KR 171210	B1		KR 1991-19468	19911102
JP 3150609	B2	Div ex	JP 1991-278407	19910930
			JP 1996-72826	19910930
CA 2488792	A1	Div ex	CA 1991-2054325	19911028
			CA 1991-2488792	19911028
CA 2054325	C		CA 1991-2054325	19911028

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 5627158	A	Div ex	US 5271941
EP 490077	B1	Related to	EP 785252
DE 69127175	E	Based on	EP 490077
ES 2104644	T3	Based on	EP 490077
US 5691317	A	Div ex	US 5271941
JP 2719060	B2	Previous Publ.	JP 06211889
JP 3150609	B2	Previous Publ.	JP 08310958

PRIORITY APPLN. INFO: US 1991-702163 19910520; US
1990-607113 19901102; US
1991-680198 19910405; US
1993-60984 19930514; US
1995-383742 19950202

AB EP 490077 A UPAB: 20050406
A 15- to 30-mer antisense oligonucleotide is complementary to a region in the first 100 N-terminal codons of RIalpha. Also 15- to 30-mer antisene oligonucleotide is a fragment of antisense DNA complementary to RIalpha.
USE/ADVANTAGE - The antisense oligonucleotides suppress RIalpha, the type I regulatory subunit of **CAMP**-dependent protein kinase, to inhibit tumour growth with no symptons of toxicity. They are used for **treating** a variety of cancers, e.g. gastric, pancreatic, lung, breast, anal, colorectal, head and neck neoplasms, neuroblastomas, melanoma and various leukaemia.
Dwg.0/5

L19 ANSWER 43 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1987-244193 [35] WPIDS
DOC. NO. CPI: C1987-103178
TITLE: Stimulating lacrimal gland secretion - by topical ocular admin. of phospho di esterase inhibitor and/or cyclic nucleotide analogues.
DERWENT CLASS: A96 B05
INVENTOR(S): DARTT, D A; GILBARD, J P

PATENT ASSIGNEE(S): (EYER-N) EYE RES INST RETINA
COUNTRY COUNT: 12
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 234854	A	19870902	(198735)*	EN	27
R: BE CH DE FR GB IT LI LU NL SE					
JP 62246524	A	19871027	(198748)		
US 4753945	A	19880628	(198828)		9
US 4956348	A	19900911	(199039)		
EP 234854	B	19910508	(199119)		
R: BE CH DE FR GB IT LI LU NL SE					
DE 3769812	G	19910613	(199125)		
JP 07088311	B2	19950927	(199543)		7

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 234854	A	EP 1987-301403	19870218
JP 62246524	A	JP 1987-33582	19870218
US 4753945	A	US 1986-830997	19860219
US 4956348	A	US 1988-211585	19880627
JP 07088311	B2	JP 1987-33582	19870218

FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 07088311	B2 Based on	JP 62246524

PRIORITY APPLN. INFO: US 1986-830997 19860219
AB EP 234854 A UPAB: 19930922
Fluid secretion of human accessory lachrimal glands is stimulated by the topical admin. to the ocular surface of a substance which causes an increase in the intracellular cyclic nucleotide level in the glands. Such substances are phosphodiesterase inhibitors and cyclic nucleotide analogues. The compsn. may opt. contain glucagon.

Phosphodiesterase inhibitors include 3-(isobutyl-1-methylxanthine, theophylline, caffeine, methylxanthine and theobromine. Cyclic nucleotide analogues include 8-bromo-**cAMP**, dibutyl **cAMP**, **adenosine** 3',5'-**cyclic phosphorothioate** and 8-bromo cGMP.

USE - Stimulation of lachrimal secretion is used for **treating** 'Dry' eye disorders such as keratoconjunctivitis sicca, Stevens-Johnson syndrome, ocular cicatricial pemphigoid slepharitis, neurotrophic ocular surface disease, corneal exposure and ocular problems caused by wearing contact lenses.
0/1

=> => □

=> fil medline
FILE 'MEDLINE' ENTERED AT 12:33:28 ON 09 MAY 2005

FILE LAST UPDATED: 6 MAY 2005 (20050506/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

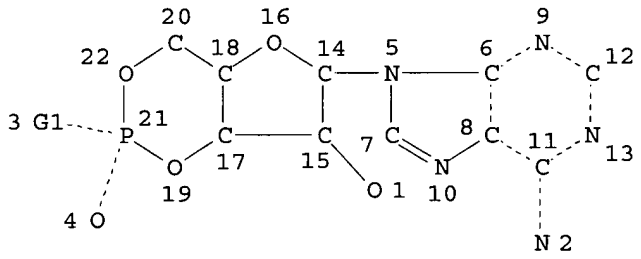
http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

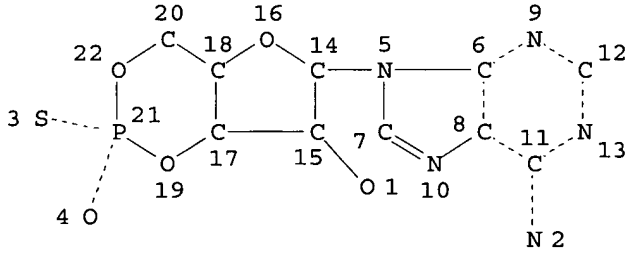
=> d que l22
L1 STR



VAR G1=O/S
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L2 (955)SEA FILE=REGISTRY SSS FUL L1
L3 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

```
L4          63 SEA FILE=REGISTRY SUB=L2 SSS FUL L3
L5         396 SEA FILE=MEDLINE ABB=ON  PLU=ON  L4
L7        4036 SEA FILE=MEDLINE ABB=ON  PLU=ON  ?PHOSPHOROTHIOATE?
L9       64337 SEA FILE=MEDLINE ABB=ON  PLU=ON  CYCLIC AMP+NT/CT
L13        414 SEA FILE=MEDLINE ABB=ON  PLU=ON  L9 (L) TU./CT
L20        596 SEA FILE=MEDLINE ABB=ON  PLU=ON  L7 AND L9
L21        396 SEA FILE=MEDLINE ABB=ON  PLU=ON  L20 AND L5
L22         10 SEA FILE=MEDLINE ABB=ON  PLU=ON  L21 AND L13


=> d .med rn l22 1-10

L22  ANSWER 1 OF 10     MEDLINE on STN
AN   2004638833     MEDLINE
DN   PubMed ID: 15537737
TI   Cerebellar norepinephrine modulates learning of delay classical eyeblink
     conditioning: evidence for post-synaptic signaling via PKA.
AU   Cartford M Claire; Samec Amy; Fister Mathew; Bickford Paula C
CS   James A. Haley Veterans Administration Hospital, Tampa, Florida 33612,
     USA.
NC   AG04418 (NIA)
SO   Learning & memory (Cold Spring Harbor, N.Y.), (2004 Nov-Dec) 11 (6) 732-7.
     Electronic Publication: 2004-11-10.
     Journal code: 9435678. ISSN: 1072-0502.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200503
ED   Entered STN: 20041224
     Last Updated on STN: 20050316
     Entered Medline: 20050315
AB   The neurotransmitter norepinephrine (NE) has been shown to modulate
     cerebellar-dependent learning and memory.  Lesions of the nucleus locus
     coeruleus or systemic blockade of noradrenergic receptors has been shown
     to delay the acquisition of several cerebellar-dependent learning tasks.
     To date, no studies have shown a direct involvement of cerebellar
     noradrenergic activity nor localized the post-synaptic response to
     cerebellar beta-noradrenergic receptor signaling.  Using ipsilateral,
     localized infusions into cerebellar lobule HVI and interpositus (IP), we
     have established that blocking beta-noradrenergic receptors with
     propranolol significantly impairs acquisition of conditioned responses.
     Furthermore, interrupting activation of cAMP-dependent PKA in the
     cerebellum using Rp-cAMPS completely prevents acquisition.  However,
     neither blocking beta-adrenergic receptors nor blocking PKA activation
     significantly interferes with performance of established conditioned
     responses when administered after the learned response is formed.
CT   Check Tags: Comparative Study; Male
      Adrenergic beta-Antagonists: AD, administration & dosage
      Analysis of Variance
      Animals
      Cerebellum: CY, cytology
      Cerebellum: DE, drug effects
     *Cerebellum: ME, metabolism
      Conditioning, Eyelid: DE, drug effects
     *Conditioning, Eyelid: PH, physiology
        Cyclic AMP: AD, administration & dosage
       *Cyclic AMP: AA, analogs & derivatives
      Cyclic AMP-Dependent Protein Kinases: AI, antagonists & inhibitors
     *Cyclic AMP-Dependent Protein Kinases: PH, physiology
```

Microinjections
Neurons: DE, drug effects
Neurons: ME, metabolism
*Norepinephrine: ME, metabolism
Propranolol: AD, administration & dosage
Protein Kinase Inhibitors: AD, administration & dosage
Rats
Rats, Inbred F344
Reaction Time: DE, drug effects
Reaction Time: PH, physiology
Research Support, U.S. Gov't, Non-P.H.S.
Research Support, U.S. Gov't, P.H.S.
Signal Transduction: DE, drug effects
Signal Transduction: PH, physiology
Synaptic Transmission: DE, drug effects
*Synaptic Transmission: PH, physiology
Thionucleotides: AD, administration & dosage
Time Perception: DE, drug effects
Time Perception: PH, physiology

RN **23645-17-2 (adenosine-3',5'-cyclic phosphorothioate)**; 51-41-2 (Norepinephrine); 525-66-6 (Propranolol); 60-92-4 (Cyclic AMP)

L22 ANSWER 2 OF 10 MEDLINE on STN
AN 2003545368 MEDLINE
DN PubMed ID: 14622586
TI Dysregulation of protein kinase a signaling in the aged prefrontal cortex: new strategy for treating age-related cognitive decline.
CM Comment in: Neuron. 2003 Nov 13;40(4):669-70. PubMed ID: 14622572
AU Ramos Brian P; Birnbaum Shari G; Lindenmayer Isabelle; Newton Samuel S; Duman Ronald S; Arnsten Amy F T
CS Department of Neurobiology, Yale University School of Medicine, New Haven, CT 06510, USA.
NC AG06036 (NIA)
MH45481 (NIMH)
SO Neuron, (2003 Nov 13) 40 (4) 835-45.
Journal code: 8809320. ISSN: 0896-6273.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 20031120
Last Updated on STN: 20040114
Entered Medline: 20040113
AB Activation of the cAMP/protein kinase A (PKA) pathway has been proposed as a mechanism for improving age-related cognitive deficits based on studies of hippocampal function. However, normal aging also afflicts prefrontal cortical cognitive functioning. Here, we report that agents that increase PKA activity impair rather than improve prefrontal cortical function in aged rats and monkeys with prefrontal cortical deficits. Conversely, PKA inhibition ameliorates prefrontal cortical cognitive deficits. Western blot and immunohistochemical analyses of rat brain further indicate that the cAMP/PKA pathway becomes disinhibited in the prefrontal cortex with advancing age. These data demonstrate that PKA inhibition, rather than activation, is the appropriate strategy for restoring prefrontal cortical cognitive abilities in the elderly.
CT Check Tags: Male
3',5'-Cyclic-Nucleotide Phosphodiesterase: AI, antagonists & inhibitors
3',5'-Cyclic-Nucleotide Phosphodiesterase: ME, metabolism
Aging: DE, drug effects

*Aging: ME, metabolism
Animals
Cognition Disorders: DT, drug therapy
*Cognition Disorders: EN, enzymology
Cognition Disorders: PP, physiopathology
***Cyclic AMP: AA, analogs & derivatives**
Cyclic AMP: PD, pharmacology
Cyclic AMP: TU, therapeutic use
Cyclic AMP-Dependent Protein Kinases: AI, antagonists & inhibitors
*Cyclic AMP-Dependent Protein Kinases: ME, metabolism
DNA-Binding Protein, Cyclic AMP-Responsive: ME, metabolism
Enzyme Inhibitors: PD, pharmacology
Macaca mulatta
Memory Disorders: DT, drug therapy
*Memory Disorders: EN, enzymology
Memory Disorders: PP, physiopathology
Nootropic Agents: PD, pharmacology
Phosphodiesterase Inhibitors: PD, pharmacology
Phosphodiesterase Inhibitors: TU, therapeutic use
Prefrontal Cortex: DE, drug effects
*Prefrontal Cortex: EN, enzymology
Prefrontal Cortex: PP, physiopathology
Rats
Rats, Sprague-Dawley
Research Support, U.S. Gov't, P.H.S.
Rolipram: PD, pharmacology
Rolipram: TU, therapeutic use
Thionucleotides: PD, pharmacology
Thionucleotides: TU, therapeutic use
Up-Regulation: DE, drug effects
Up-Regulation: PH, physiology

RN **23645-17-2 (adenosine-3',5'-cyclic phosphorothioate)**; 60-92-4 (Cyclic AMP); 61413-54-5 (Rolipram)

L22 ANSWER 3 OF 10 MEDLINE on STN
AN 2002729564 MEDLINE
DN PubMed ID: 12492305
TI Inhibition of protein kinase A activity interferes with long-term, but not short-term, memory of conditioned taste aversions.
AU Koh Ming Teng; Thiele Todd E; Bernstein Ilene L
CS Department of Psychology, University of Washington, Seattle 98195-1525, USA.
NC AA00258 (NIAAA)
NS37040 (NINDS)
SO Behavioral neuroscience, (2002 Dec) 116 (6) 1070-4.
Journal code: 8302411. ISSN: 0735-7044.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200301
ED Entered STN: 20021221
Last Updated on STN: 20030115
Entered Medline: 20030114
AB The present experiments examined whether inhibition of cyclic adenosine monophosphate (cAMP)-dependent protein kinase A (PKA) activity interferes with conditioned taste aversion (CTA) memories. Rats were centrally infused with the selective PKA inhibitor Rp-adenosine 3',5'-cyclic monophosphothioate triethylamine (Rp-cAMPS) before conditioning. Direct infusions of Rp-cAMPS into the amygdala showed no interference with

short-term memory but did show significant attenuation of long-term memory and more rapid extinction. Results suggest that PKA activity is involved in the consolidation of long-term memory of CTAs, and that the amygdala may be 1 site that is important for this activity.

CT Check Tags: Male
Amygdala: DE, drug effects
*Amygdala: PH, physiology
Animals
Avoidance Learning
Cyclic AMP: AD, administration & dosage
***Cyclic AMP: AA, analogs & derivatives**
Cyclic AMP: PD, pharmacology
Cyclic AMP-Dependent Protein Kinases: AI, antagonists & inhibitors
*Cyclic AMP-Dependent Protein Kinases: PD, pharmacology
Enzyme Inhibitors: AD, administration & dosage
Enzyme Inhibitors: PD, pharmacology
*Memory, Short-Term: PH, physiology
Protein Kinase Inhibitors
Rats
Rats, Long-Evans
Research Support, U.S. Gov't, P.H.S.
Stereoisomerism
Taste
Thionucleotides: AD, administration & dosage
Thionucleotides: PD, pharmacology

RN **23645-17-2 (adenosine-3',5'-cyclic phosphorothioate)**; 60-92-4 (Cyclic AMP)

L22 ANSWER 4 OF 10 MEDLINE on STN
AN 2002369689 MEDLINE
DN PubMed ID: 12114002
TI Stimulation of protein kinase a activity in the rat amygdala enhances reward-related learning.
AU Jentsch J David; Olausson Peter; Nestler Eric J; Taylor Jane R
CS Department of Psychiatry, Yale University School of Medicine, New Haven, Connecticut 06508, USA.
NC DA08227 (NIDA)
DA11026 (NIDA)
DA11717 (NIDA)
SO Biological psychiatry, (2002 Jul 15) 52 (2) 111-8.
Journal code: 0213264. ISSN: 0006-3223.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200210
ED Entered STN: 20020713
Last Updated on STN: 20021029
Entered Medline: 20021028
AB BACKGROUND: Drug addiction in humans is associated with abnormal metabolic activity within the amygdala and heightened control of behavior by drugs and drug-related (conditioned) stimuli. Drug-induced neuroadaptations, including activation of cAMP (cyclic adenosine monophosphate)-dependent protein kinase A (PKA), within the amygdala may contribute to the synaptic plasticity and reward-related learning that underlies pathologic behavior in addicted individuals. METHODS: In this study, we tested the hypothesis that stimulation of PKA activity within the rat amygdala would facilitate the acquisition of Pavlovian approach behavior, a measure of reward-related learning. RESULTS: Intraamygdala infusions of Sp-cAMPS (which activates PKA) produced concentration-dependent enhancements of the

acquisition of approach to a conditioned stimulus that predicted water availability; intraamygdala infusions of cholera toxin (which elevates cAMP levels) produced a similar effect. Conversely, intraamygdala infusions of Rp-cAMPS, an inhibitor of PKA, impaired acquisition of approach behavior. CONCLUSIONS: Together, these data demonstrate that stimulation of PKA activity in the amygdala can facilitate reward-related learning and suggest that neuroadaptative changes in the PKA pathway within this brain region may be a mechanism by which chronic drug abuse alters the control of behavior by drug-associated stimuli.

CT Check Tags: Male
Adjuvants, Immunologic: AD, administration & dosage
Amygdala: AH, anatomy & histology
*Amygdala: DE, drug effects
Analysis of Variance
Animals
Appetitive Behavior: DE, drug effects
Cholera Toxin: AD, administration & dosage
Cyclic AMP: AD, administration & dosage
***Cyclic AMP: AA, analogs & derivatives**
*Cyclic AMP-Dependent Protein Kinases: DE, drug effects
Enzyme Activation: DE, drug effects
Enzyme Inhibitors: AD, administration & dosage
*Learning: DE, drug effects
Locomotion: DE, drug effects
Rats
Rats, Sprague-Dawley
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
*Reward
Sucrose: AD, administration & dosage
Thionucleotides: AD, administration & dosage
Time Factors

RN **23645-17-2 (adenosine-3',5'-cyclic phosphorothioate)**; 57-50-1 (Sucrose); 60-92-4 (Cyclic AMP); 9012-63-9 (Cholera Toxin)

L22 ANSWER 5 OF 10 MEDLINE on STN
AN 2002096232 MEDLINE
DN PubMed ID: 11826135
TI Appetitive instrumental learning requires coincident activation of NMDA and dopamine D1 receptors within the medial prefrontal cortex.
AU Baldwin Anne E; Sadeghian Kenneth; Kelley Ann E
CS Neuroscience Training Program and Department of Psychiatry, University of Wisconsin-Madison Medical School, Madison Wisconsin 53719-1176, USA.
NC DA04788 (NIDA)
SO Journal of neuroscience : official journal of the Society for Neuroscience, (2002 Feb 1) 22 (3) 1063-71.
Journal code: 8102140. ISSN: 1529-2401.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200202
ED Entered STN: 20020205
Last Updated on STN: 20020228
Entered Medline: 20020227
AB Through its complex role in cognition, memory, and emotion, the mammalian prefrontal cortex is thought to contribute to the organization of adaptive behavioral actions. In the present studies we examined the role of dopaminergic D1 and glutamatergic NMDA receptors within the prefrontal cortex of the rat during the development of adaptive instrumental

learning. Hungry rats with bilateral indwelling cannulas aimed at the medial prefrontal cortex were trained to lever-press for food. Infusion of the selective D1 antagonist SCH-23390 (0.15, 0.3, 3.0 nmol) dose-dependently impaired acquisition of this behavior. Higher doses also impaired expression of this task. Co-infusion of the lowest dose of SCH 23390 with a low dose of the NMDA antagonist AP-5 (0.5 nmol), each of which had no effect on learning when infused alone, potently reduced the ability to acquire the response. Inhibition of intracellular protein kinase A with the selective PKA inhibitor Rp-cAMPS also disrupted acquisition, suggesting that PKA is an intracellular substrate for a D1-NMDA receptor interaction. In control experiments, drug infusions that impaired learning did not affect food intake or locomotion, suggesting a specific effect on learning. We hypothesize that coincident detection of D1-NMDA receptor activation and its transcriptional consequences, within multiple sites of a distributed corticostriatal network, may represent a conserved molecular mechanism for instrumental learning.

CT Check Tags: Male
(R)-2,3,4,5-Tetrahydro-8-chloro-3-methyl-5-phenyl-1H-3-benzazepin-7-ol: AD, administration & dosage
2-Amino-5-phosphonovalerate: AD, administration & dosage
Animals
Appetitive Behavior: DE, drug effects
*Appetitive Behavior: PH, physiology
Catheterization
Conditioning, Operant: DE, drug effects
*Conditioning, Operant: PH, physiology
Cyclic AMP: AD, administration & dosage
***Cyclic AMP: AA, analogs & derivatives**
Cyclic AMP-Dependent Protein Kinases: AI, antagonists & inhibitors
Cyclic AMP-Dependent Protein Kinases: ME, metabolism
Dopamine Antagonists: AD, administration & dosage
Dose-Response Relationship, Drug
Eating: DE, drug effects
Enzyme Inhibitors: AD, administration & dosage
Excitatory Amino Acid Antagonists: AD, administration & dosage
Locomotion: DE, drug effects
Microinjections
Prefrontal Cortex: CY, cytology
*Prefrontal Cortex: ME, metabolism
Rats
Rats, Sprague-Dawley
Receptors, Dopamine D1: AI, antagonists & inhibitors
*Receptors, Dopamine D1: ME, metabolism
Receptors, N-Methyl-D-Aspartate: AI, antagonists & inhibitors
*Receptors, N-Methyl-D-Aspartate: ME, metabolism
Research Support, U.S. Gov't, P.H.S.
Thionucleotides: AD, administration & dosage

RN **23645-17-2 (adenosine-3',5'-cyclic phosphorothioate)**; 60-92-4 (Cyclic AMP); 76726-92-6 (2-Amino-5-phosphonovalerate); 87075-17-0 ((R)-2,3,4,5-Tetrahydro-8-chloro-3-methyl-5-phenyl-1H-3-benzazepin-7-ol)

L22 ANSWER 6 OF 10 MEDLINE on STN
AN 2001106696 MEDLINE
DN PubMed ID: 11090612
TI Phosphorylated cAMP response element-binding protein as a molecular marker of memory processing in rat hippocampus: effect of novelty.
AU Viola H; Furman M; Izquierdo L A; Alonso M; Barros D M; de Souza M M; Izquierdo I; Medina J H
CS Instituto de Biologia Celular y Neurociencias, Facultad de Medicina, Universidad de Buenos Aires, Paraguay 2155, piso 3, 1121 Buenos Aires,

Argentina.
SO Journal of neuroscience : official journal of the Society for Neuroscience, (2000 Dec 1) 20 (23) RC112.
Journal code: 8102140. ISSN: 1529-2401.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200102
ED Entered STN: 20010322
Last Updated on STN: 20010521
Entered Medline: 20010208
AB From mollusks to mammals the activation of cAMP response element-binding protein (CREB) appears to be an important step in the formation of long-term memory (LTM). Here we show that a 5 min exposure to a novel environment (open field) 1 hr after acquisition of a one-trial inhibitory avoidance training hinders both the formation of LTM for the avoidance task and the increase in the phosphorylation state of hippocampal Ser 133 CREB [phosphorylated CREB (pCREB)] associated with the avoidance training. To determine whether this LTM deficit is attributable to the reduced pCREB level, rats were bilaterally cannulated to deliver Sp-adenosine 3', 5'-cyclic monophosphothioate (Sp-cAMPS), an activator of PKA. Infusion of Sp-Adenosine 3',5'-cyclic monophosphothioate Sp-cAMPS to CA1 region increased hippocampal pCREB levels and restored normal LTM of avoidance learning in rats exposed to novelty. Moreover, a 5 min exposure to the open field 10 min before the avoidance training interferes with the amnesic effect of a second 5 min exposure to the open field 1 hr after avoidance training and restores the hippocampal levels of pCREB. In contrast, the avoidance training-associated activation of extracellular signal-regulated kinases (p42 and p44 mitogen-activated protein kinases) in the hippocampus is not altered by novelty. Together, these findings suggest that novelty regulates LTM formation by modulating the phosphorylation state of CREB in the hippocampus.
CT Check Tags: Male
Amnesia, Retrograde: DT, drug therapy
Amnesia, Retrograde: ME, metabolism
Animals
Avoidance Learning: DE, drug effects
Avoidance Learning: PH, physiology
Behavior, Animal: DE, drug effects
Behavior, Animal: PH, physiology
Biological Markers
Cyclic AMP: AD, administration & dosage
***Cyclic AMP: AA, analogs & derivatives**
Cyclic AMP-Dependent Protein Kinases: ME, metabolism
*DNA-Binding Protein, Cyclic AMP-Responsive: ME, metabolism
Exploratory Behavior: DE, drug effects
Exploratory Behavior: PH, physiology
Hippocampus: CH, chemistry
Hippocampus: DE, drug effects
Hippocampus: ME, metabolism
*Hippocampus: PH, physiology
Infusions, Parenteral
Memory: DE, drug effects
*Memory: PH, physiology
Microinjections
Mitogen-Activated Protein Kinase 1: ME, metabolism
Mitogen-Activated Protein Kinase 3
Mitogen-Activated Protein Kinases: ME, metabolism
Phosphorylation: DE, drug effects

Rats
Rats, Wistar
Research Support, Non-U.S. Gov't
Retention (Psychology): DE, drug effects
Retention (Psychology): PH, physiology
Thionucleotides: AD, administration & dosage
Time
RN **23645-17-2 (adenosine-3',5'-cyclic phosphorothioate)**; 60-92-4 (Cyclic AMP)

L22 ANSWER 7 OF 10 MEDLINE on STN
AN 2001062995 MEDLINE
DN PubMed ID: 11103888
TI Conditioned locomotion in rats following amphetamine infusion into the nucleus accumbens: blockade by coincident inhibition of protein kinase A.
AU Sutton M A; McGibney K; Beninger R J
CS Department of Psychology, Queen's University, Kingston, Ontario, Canada.
SO Behavioural pharmacology, (2000 Aug) 11 (5) 365-76.
Journal code: 9013016. ISSN: 0955-8810.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200012
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001228
AB Recent studies demonstrate a role for cyclic adenosine monophosphate (cAMP)-dependent protein kinase (PKA) in the nucleus accumbens (NAc) in reward-related learning. To clarify this role, we assessed the effect of PKA inhibition on the unconditioned and conditioned locomotor activating properties of intra-NAc amphetamine. Rats underwent three 60 min conditioning sessions, pairing a test environment with bilateral co-infusions of amphetamine (25 microg/side) and the PKA inhibitor Rp-adenosine 3',5'-cyclic monophosphothioate triethylamine (Rp-cAMPS) (0, 2.5, 250, 500 ng, 1, 10 or 20 microg/side). Two additional groups - receiving amphetamine explicitly unpaired with the environment or saline/environment pairings - served as controls. In a subsequent drug-free 60 min session, animals that received amphetamine/environment pairings demonstrated conditioned locomotion relative to controls. Rp-cAMPS co-treatment during pairing sessions differentially affected conditioned and unconditioned locomotor activation. Amphetamine-induced unconditioned activity was significantly enhanced by 500 ng and 1 microg Rp-cAMPS, locomotor sensitization was enhanced by 250 ng-1 microg Rp-cAMPS, and conditioned activity was attenuated by 1 microg Rp-cAMPS and blocked by 10 and 20 microg Rp-cAMPS. Thus, unconditioned activity and locomotor sensitization were enhanced at doses (250 ng-1 microg) that did not affect or attenuated conditioned activity, while conditioned activity was reduced or blocked at doses (1-20 microg) that enhanced or did not affect overall unconditioned activity. These results demonstrate that the activation of PKA plays a critical role in the process by which properties of drugs become associated with environmental stimuli.
CT Check Tags: Male
Amphetamine: AD, administration & dosage
*Amphetamine: PD, pharmacology
Animals
Central Nervous System Stimulants: AD, administration & dosage
*Central Nervous System Stimulants: PD, pharmacology
Conditioning, Classical
Cyclic AMP: AD, administration & dosage

***Cyclic AMP: AA, analogs & derivatives**
Cyclic AMP: PD, pharmacology
*Cyclic AMP-Dependent Protein Kinases: ME, metabolism
Enzyme Inhibitors: AD, administration & dosage
Enzyme Inhibitors: PD, pharmacology
*Locomotion: DE, drug effects
*Nucleus Accumbens: DE, drug effects
Nucleus Accumbens: PH, physiology
Rats
Rats, Wistar
Research Support, Non-U.S. Gov't
Thionucleotides: AD, administration & dosage
Thionucleotides: PD, pharmacology
RN **23645-17-2 (adenosine-3',5'-cyclic phosphorothioate)**; 300-62-9 (Amphetamine); 60-92-4 (Cyclic AMP)

L22 ANSWER 8 OF 10 MEDLINE on STN
AN 2001056971 MEDLINE
DN PubMed ID: 10905623
TI Differential role of hippocampal cAMP-dependent protein kinase in short- and long-term memory.
AU Vianna M R; Izquierdo L A; Barros D M; Ardenghi P; Pereira P; Rodrigues C; Moletta B; Medina J H; Izquierdo I
CS Centro de Memoria, Departamento de Bioquimica, Instituto de Ciencias Basicas da Saude, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil.
SO Neurochemical research, (2000 May) 25 (5) 621-6.
Journal code: 7613461. ISSN: 0364-3190.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200012
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001220
AB One-trial step-down inhibitory (passive) avoidance training is followed by two peaks of cAMP-dependent protein kinase (PKA) activity in rat CA1: one immediately after training and the other 3 h later. The second peak relies on the first: Immediate posttraining infusion into CA1 of the inhibitor of the regulatory subunit of PKA, Rp-cAMPS, at a dose that reduces PKA activity during less than 90 min, cancelled both peaks. Long-term memory (LTM) of this task measured at 24 h depends on the two peaks: Rp-cAMPS given into CA1 0 or 175 min posttraining, but not between those times, blocked LTM. However, the effect of immediate posttraining Rp-cAMPS on LTM could not be reversed by the activator of the regulatory subunit of PKA, Sp-cAMPS, given at 180 min, which suggests that, for LTM, the first peak may be more important than the second. When given at 0, 22, 45, or 90, but not at 175 min from training, Rp-cAMPS blocked short-term memory (STM) measured at 90 or 180 min. This effect of immediate posttraining Rp-cAMPS infusion on STM but not that on LTM was readily reversed by Sp-cAMPS infused 22 min later. On its own, Sp-cAMPS had effects exactly opposite to those of the inhibitor. It enhanced LTM when given at 0 or 175 min from training, and it enhanced STM when given at 0, 22, 45, or 90 min from training. These findings show that STM and LTM formation require separate PKA-dependent processes in CA1. STM relies on the continued activity of the enzyme during the first 90 min. LTM relies on the two peaks of PKA activity that occur immediately and 180 min posttraining.
CT Animals

Avoidance Learning: DE, drug effects
*Avoidance Learning: PH, physiology
Cyclic AMP: AD, administration & dosage
***Cyclic AMP: AA, analogs & derivatives**
Cyclic AMP: PD, pharmacology
*Cyclic AMP-Dependent Protein Kinases: ME, metabolism
Electroshock
Enzyme Inhibitors: AD, administration & dosage
Enzyme Inhibitors: PD, pharmacology
Hippocampus: DE, drug effects
Hippocampus: EN, enzymology
*Hippocampus: PH, physiology
Infusions, Parenteral
Memory: DE, drug effects
*Memory: PH, physiology
Memory, Short-Term: DE, drug effects
*Memory, Short-Term: PH, physiology
Neurons: DE, drug effects
Neurons: EN, enzymology
Neurons: PH, physiology
Rats
Rats, Wistar
Research Support, Non-U.S. Gov't
Thionucleotides: AD, administration & dosage
*Thionucleotides: PD, pharmacology
Time Factors

RN **23645-17-2 (adenosine-3',5'-cyclic phosphorothioate)**; 60-92-4 (Cyclic AMP)

L22 ANSWER 9 OF 10 MEDLINE on STN
AN 97361323 MEDLINE
DN PubMed ID: 9218217
TI Activation of f-channels by cAMP analogues in macropatches from rabbit sino-atrial node myocytes.
AU Bois P; Renaudon B; Baruscotti M; Lenfant J; DiFrancesco D
CS Universite de Poitiers, Laboratoire de Physiologie Generale, UMR 6558, France.
SO Journal of physiology, (1997 Jun 15) 501 (Pt 3) 565-71.
Journal code: 0266262. ISSN: 0022-3751.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
ED Entered STN: 19970922
Last Updated on STN: 19970922
Entered Medline: 19970909
AB 1. The action of the two diastereometric **phosphorothioate** derivatives of cAMP, Rp-cAMPs and Sp-cAMPs, was investigated on hyperpolarization-activated 'pacemaker' current (i(f)) recorded in inside-out macropatches from rabbit sino-atrial (SA) node myocytes. 2. When superfused on the intracellular side of f-channels at the concentration of 10 microM, both cAMP derivatives accelerated i(f) activation; their action was moderately less pronounced than that due to the same concentration of cAMP. 3. The measurement of the i(f) conductance-voltage relation by voltage ramp protocols indicated that both cAMP analogues shift the activation curve of i(f) to more positive voltages with no change in maximal (fully activated) conductance. 4. Dose-response relationships of the shift of the i(f) activation curve showed that both Rp-cAMPs and Sp-cAMPs act as agonists in the

cAMP-dependent direct f-channel activation. Fitting data to the Hill equation resulted in maximal shifts of 9.6 and 9.5 mV, apparent dissociation constants of 0.82 and 5.4 microM, and Hill coefficients of 0.82 and 1.12 for Sp-cAMPs and Rp-cAMPs, respectively. 5. The activating action of Rp-cAMPs, a known antagonist of cAMP in the activation of cAMP-dependent protein kinase, confirms previously established evidence that f-channel activation does not involve phosphorylation. These results also suggest that the cAMP binding site of f-channels may be structurally similar to the cyclic nucleotide binding site of olfactory receptor channels.

CT Check Tags: In Vitro
Animals
Binding Sites
Cyclic AMP: AD, administration & dosage
***Cyclic AMP: AA, analogs & derivatives**
Cyclic AMP: PD, pharmacology
Dose-Response Relationship, Drug
*Ion Channels: DE, drug effects
*Ion Channels: ME, metabolism
Membrane Potentials
Perfusion
Rabbits
Research Support, Non-U.S. Gov't
Sinoatrial Node: CY, cytology
*Sinoatrial Node: DE, drug effects
*Sinoatrial Node: ME, metabolism
Thionucleotides: AD, administration & dosage
*Thionucleotides: PD, pharmacology

RN **23645-17-2 (adenosine-3',5'-cyclic phosphorothioate)**; 60-92-4 (Cyclic AMP)

L22 ANSWER 10 OF 10 MEDLINE on STN
AN 89153387 MEDLINE
DN PubMed ID: 2537746
TI Rp-diastereomer of adenosine cyclic 3',5'-**phosphorothioate** as an antagonist of the stimulatory action of cyclic AMP on the ouabain-insensitive Na efflux in single barnacle muscle fibers.
AU Nwoga J; Bittar E E
CS Department of Physiology, University of Wisconsin, Madison 53706.
SO Experientia, (1989 Feb 15) 45 (2) 142-3.
Journal code: 0376547. ISSN: 0014-4754.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198904
ED Entered STN: 19900306
Last Updated on STN: 19970203
Entered Medline: 19890410
AB Single muscle fibers of the barnacle Balanus nubilus have been used as a preparation to test the possibility that the Rp-diastereomer of adenosine cyclic 3',5'-**phosphorothioate**, which is the first available analog of cAMP that acts as an antagonist of cAMP, may reduce the magnitude of cAMP-mediated stimulation of the resting ouabain-insensitive Na efflux. The results obtained show that this antagonist is, in fact, able to reduce stimulation of the Na efflux by injected cAMP in a dose-dependent manner.
CT Animals
Biological Transport: DE, drug effects
Cyclic AMP: AD, administration & dosage

***Cyclic AMP: AA, analogs & derivatives**
***Cyclic AMP: AI, antagonists & inhibitors**
Cyclic AMP: PD, pharmacology
Dose-Response Relationship, Drug
Kinetics
Muscles: DE, drug effects
*Muscles: ME, metabolism
*Ouabain: PD, pharmacology
*Sodium: ME, metabolism
Stereoisomerism
Thionucleotides: AD, administration & dosage
*Thionucleotides: PD, pharmacology
Thoracica: DE, drug effects
*Thoracica: ME, metabolism
RN **23645-17-2 (adenosine-3',5'-cyclic phosphorothioate)**; 60-92-4 (Cyclic AMP); 630-60-4 (Ouabain); 7440-23-5 (Sodium)

=>

Amy Bowman 10/428,458

```
FILE 'HOME' ENTERED AT 12:43:15 ON 09 MAY 2005)

     FILE 'REGISTRY' ENTERED AT 12:43:54 ON 09 MAY 2005
                ACT BERCH338/A
               ---------
L1              STR
L2   (       505)SEA FILE=REGISTRY SSS FUL L1
L3              STR
L4           136 SEA FILE=REGISTRY SUB=L2 SSS FUL L3
               ---------
                ACT BERCH338PROV/A
               ---------
L5              STR
L6   (       505)SEA FILE=REGISTRY SSS FUL L5
L7              STR
L8            23 SEA FILE=REGISTRY SUB=L6 SSS FUL L7
               ---------
L9           113 S L4 NOT L8
L10            3 S L9 NOT (CAPLUS OR CA OR CAOLD OR USPATFULL)/LC

     FILE 'HCAPLUS' ENTERED AT 12:46:02 ON 09 MAY 2005
L11           33 S L9

     FILE 'REGISTRY' ENTERED AT 12:46:21 ON 09 MAY 2005

     FILE 'HCAPLUS' ENTERED AT 12:46:47 ON 09 MAY 2005

=> d cost
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CONNECT CHARGES                                   2.39       6.78
NETWORK CHARGES                                   0.06       0.48
SEARCH CHARGES                                    0.00      18.40
DISPLAY CHARGES                                 173.58     179.10
                                               -------    -------
FULL ESTIMATED COST                             176.03     204.76

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                             -24.09     -24.09

IN FILE 'HCAPLUS' AT 12:47:33 ON 09 MAY 2005


=>
```